下脂肪厚の基準値として採用した．測定時の被験者の姿勢，皮下脂肪厚の測定と分析の方法はAbe et al.[5)]の報告において採用されているものと同一とした．すなわち，測定時の被験者の姿勢は安静立位であり，超音波ゼリー（エコーゼリー，Aloka 社製）を塗布したプローブを被験者の皮膚に対して直角に接触させ，プローブの皮膚への圧迫による画像のゆがみが生じていないことを確認した上で得られた画像より，皮膚表面から皮下脂肪と筋との境界線を結ぶ直線距離を皮下脂肪厚として測定した．測定箇所は形態計測にてマーキングした４箇所であり，測定時の超音波発信周波数は7.5 mHzであった．測定は，同一被検者に対し原則として２回行い，皮下脂肪厚の測定値が１mm以上ずれた場合には再度測定した．

４．BI法によるRおよびXの測定

株式会社タニタより貸与された小型の局所インピーダンス計測器（**図１**）を利用して，RおよびXを測定した．計測器の１辺には，２cmの間隔をおいて一対の電流印加電極と電圧計測電極が敷設されてあった．測定時の被験者の姿勢は安静立位であり，測定部は超音波法と同一であった．通電性を高めるため，水を含ませたスポンジに計測器の電極を押し付けて湿らせ，その直後に電極を３秒ほど皮膚に押しつけることにより，RおよびXを測定した．赤外線を利用して，計測器が測定した値を表示機に読み取らせ，記録した．測定に用いた周波数は50 kHz，電流は500μAであった．RとXの測定は同一被検者に対し２回行った．なお，本研究の予備実験において，腹部におけるRおよびXの測定値には呼吸が影響していることが確認されたため，超音波法，インピーダンス法ともに，被験者には，腹部皮下脂肪厚の測定時に10秒程度の息止めを指示した．

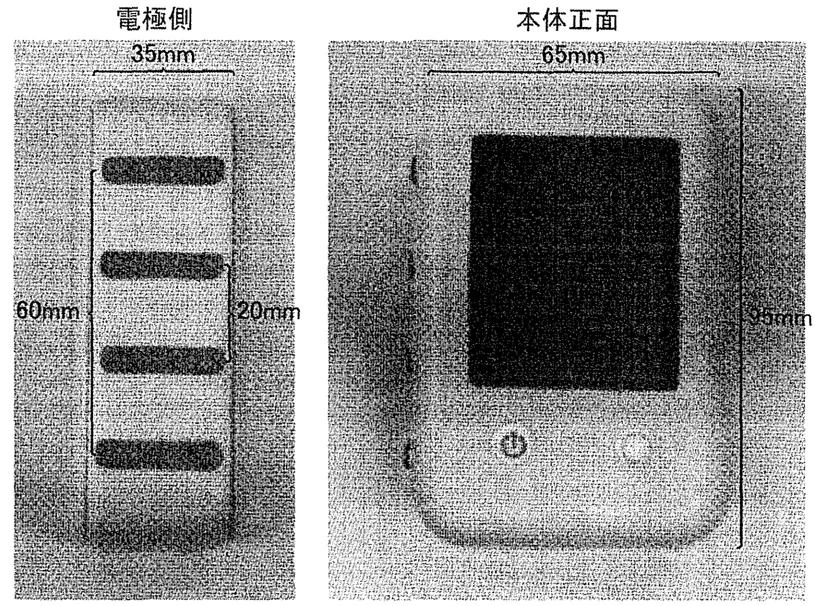

図１　局所インピーダンス計測器

５．再現性

超音波法による皮下脂肪厚測定値ならびにBI法によるR，Xの再現性については，23～33歳の男女８名を対象に，２～３日の間隔をおいて検討した．両測定日における測定値の級内相関は，皮下脂肪厚は0.998，Rは0.996，Xは0.996，R / Xは0.972であった．変動係数は，皮下脂肪厚は2.9 %，Rは3.0 %，Xは4.8 %，R / Xは6.9 %であった．いずれも，測定値に有意な日間差は認められなかった．

６．統計

本研究における各測定値は平均値と標準誤差により示した．４部位より測定したR / Xと皮下脂肪厚との相関関係を男女別に検討し，その傾きおよび切片における性差および部位差の有無を共分散分析によって確認した．これらの回帰式の傾きおよび切片における有意差が認められなかった場合に，作成した推定式を他者に適用する妥当性を確認するため，被験者をグループⅠおよびグループⅡへと無作為に分類した．グループⅠのデータを用いて，超音波法により測定した皮下脂肪厚を従属変数に，R / Xを独立変数とした推定式を作成した．さらに，推定値と基準値の偏差平方和と回帰式の切片および傾きから t 統計量を算出し，回帰式がY＝Xと有意に異なるか否かの検定を行った．推定値と基準値における系統誤差の有無は，両者の平均値と残差との間における相関係数の有意性より(Bland and Altman 1986)[12)] 判断した．また，皮下脂肪厚の推定値の標準誤差(SEE)も算出した．いずれの場合も，有意水準は５％とした．

結　果

全被験者の全部位を対象としたR / Xと皮下脂肪厚との関係を**図２A～D**に示した．男女とも，全部位において，両者の間には有意な正の相関が認められた（男性：r＝0.778～0.909，女性：r＝0.820～0.867，いずれも $p<0.05$）．また，共分散分析の結果，R / Xと皮下脂肪厚との関係における回帰式の傾きおよび切片には有意な部位差ならびに性差が確認されなかったため，被験

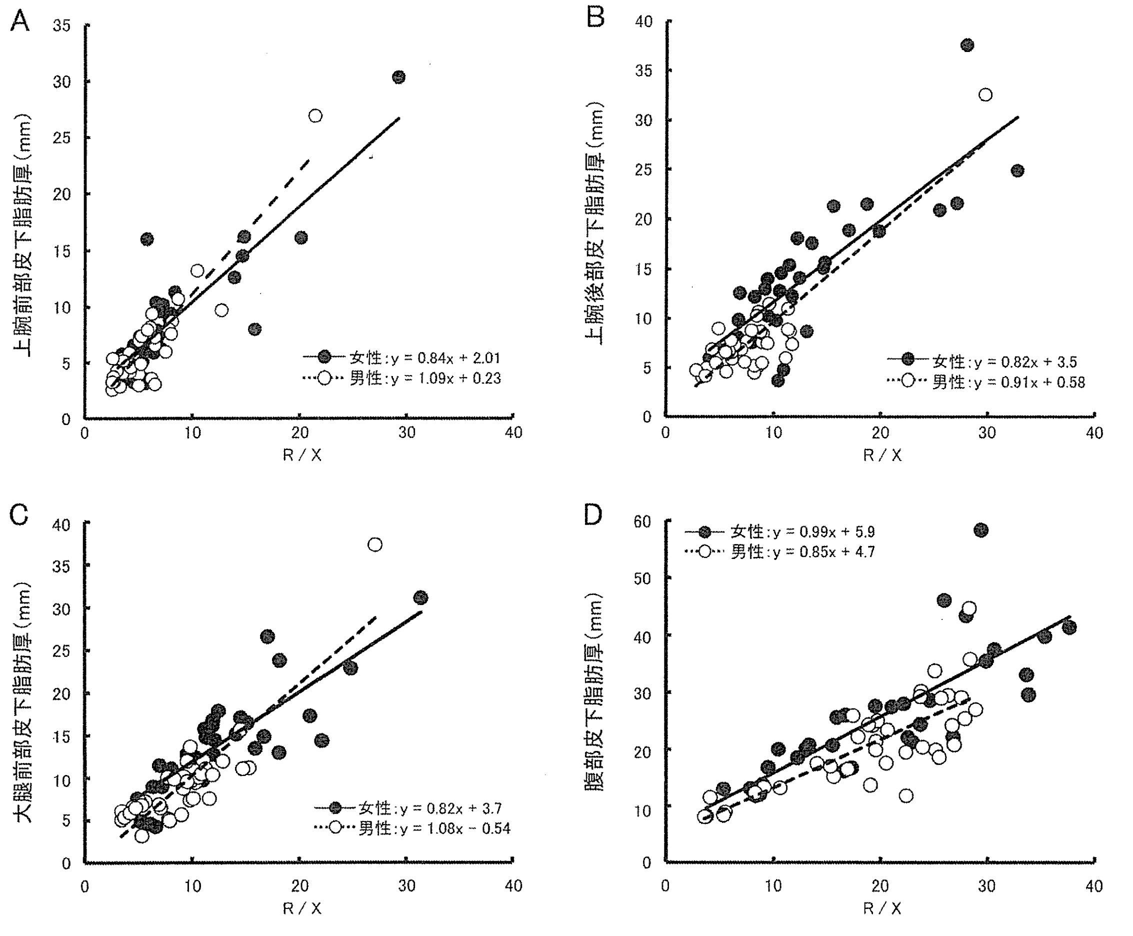

図2　全被験者におけるR/Xと各皮下脂肪厚との関係
A:上腕前部, B:上腕後部, C:大腿前部, D:腹部

表2　両群における被験者の身体的情報

	グループⅠ(n=35)		グループⅡ(n=36)	
	平均値	標準誤差	平均値	標準誤差
女性人数	15		18	
年齢(歳)	41.0	2.2	45.8 *	2.3
身長(cm)	164.3	1.6	163.4	1.4
体重(kg)	63.1	2.5	64.2	1.7
BMI (kg/m^2)	23.1	0.6	24.0	0.5
皮下脂肪厚(mm)				
上腕前部	7.9	1.2	7.2	0.6
上腕後部	11.2	1.3	10.2	0.9
大腿前部	12.6	1.0	10.6	0.8
腹部	23.0	1.6	23.5	1.8
R/X				
上腕前部	6.8	1.0	6.8	0.7
上腕後部	10.4	1.2	10.0	0.9
大腿前部	11.3	0.9	10.4	0.8
腹部	19.5	1.4	19.7	1.5

* $p < 0.05$

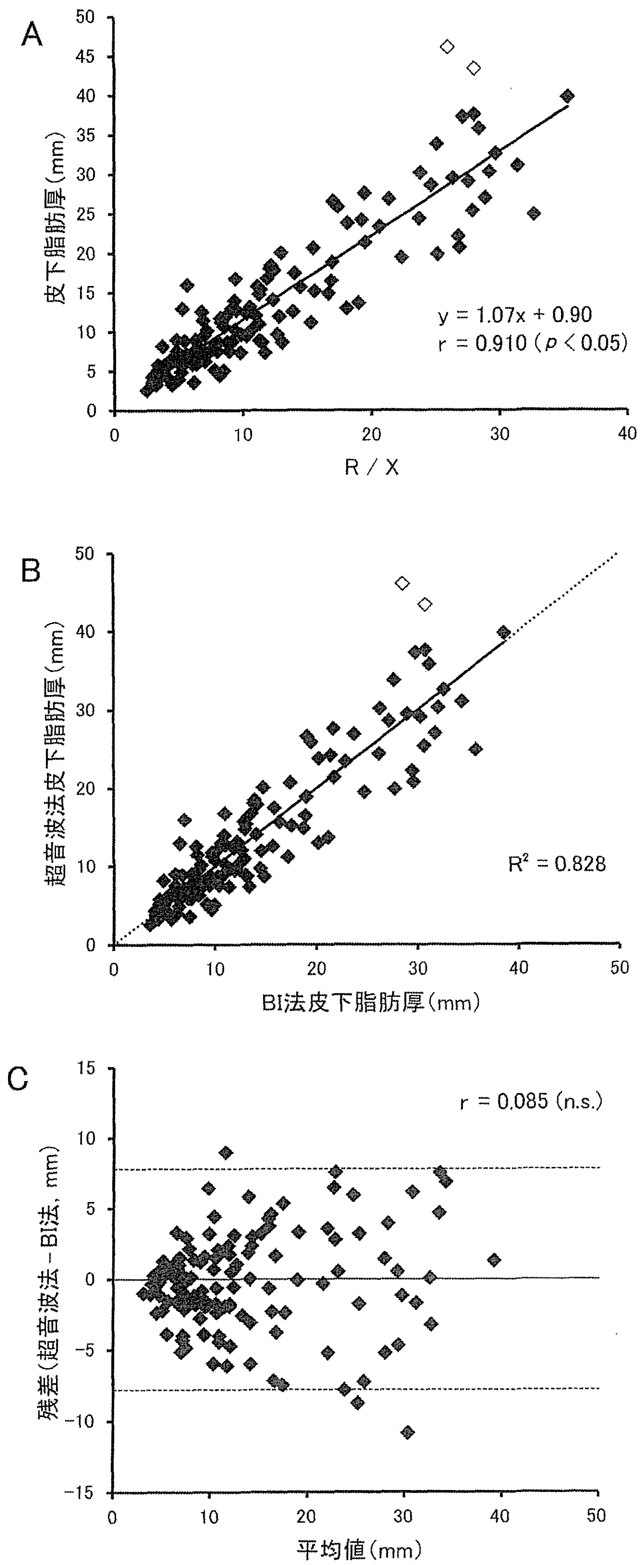

図3　グループⅠにおける推定結果

A：R/Xと皮下脂肪厚の関係，B：皮下脂肪厚の基準値と推定値との関係(点線はY＝X)，C：系統誤差の確認(点線は±2SD)
なお，皮下脂肪厚が43 mm以上の箇所(図3Aと図3Bにおける白抜きプロット)は，図3Cの分析から除外した．

者をグループⅠならびにグループⅡの2群へと無作為に分類した．グループⅠとグループⅡの身体的特徴を**表2**に示した．グループⅡにおける年齢がグループⅠのそれに比べ有意に高い値を示したが，それ以外の項目においては有意差が認められなかった．

図3に，グループⅠにおけるR/Xと皮下脂肪厚との関係，皮下脂肪厚の推定値と基準値との関係，ならびにBland-Altman plot[12]を示した．R/Xと皮下脂肪厚との間には有意な正の相関が認められた(r＝0.910, $p<0.05$, **図3A**)．この関係式により得られたy＝1.07×0.90(y：皮下脂肪厚，x：R/X)によりグループⅠの全被験者における皮下脂肪厚を推定した結果，推定値(13.7±8.6 mm)と基準値(13.7±9.4 mm)の相関における決定係数は0.828，SEEは3.6 mmであった．両者の関係から求めた回帰直線はY＝Xとの間に有意差がなかった(**図3B**)．Bland-Altman plot[12]の結果，皮下脂肪厚が高値を示すほど過小評価される(r＝0.223, $p<0.05$)ことが確認されたが，皮下脂肪厚が43 mm以上となった腹部のデータ2名分を除外するとこの相関の有意性は消失し(r＝0.085, n.s., **図3C**)，SEEも3.3 mmへと低下した．

グループⅠのデータを用いて作成された推定式をグループⅡに適用したところ，皮下脂肪厚の推定値(12.9±9.1 mm)と基準値(13.4±8.3 mm)との相関における決定係数は0.773，SEEは3.9 mmであった(**図4A**)．また，両者の関係から求めた回帰直線はY＝Xとの間に有意差がなかった．皮下脂肪厚が高い値を示す個人ほど過小評価される(r＝0.242, $p<0.05$)ことが確認されたが，グループⅠと同様に，皮下脂肪厚が43 mm以上となった腹部のデータ2名分を除外するとこの相関の有意性は消失し(r＝－0.007, n.s., 図

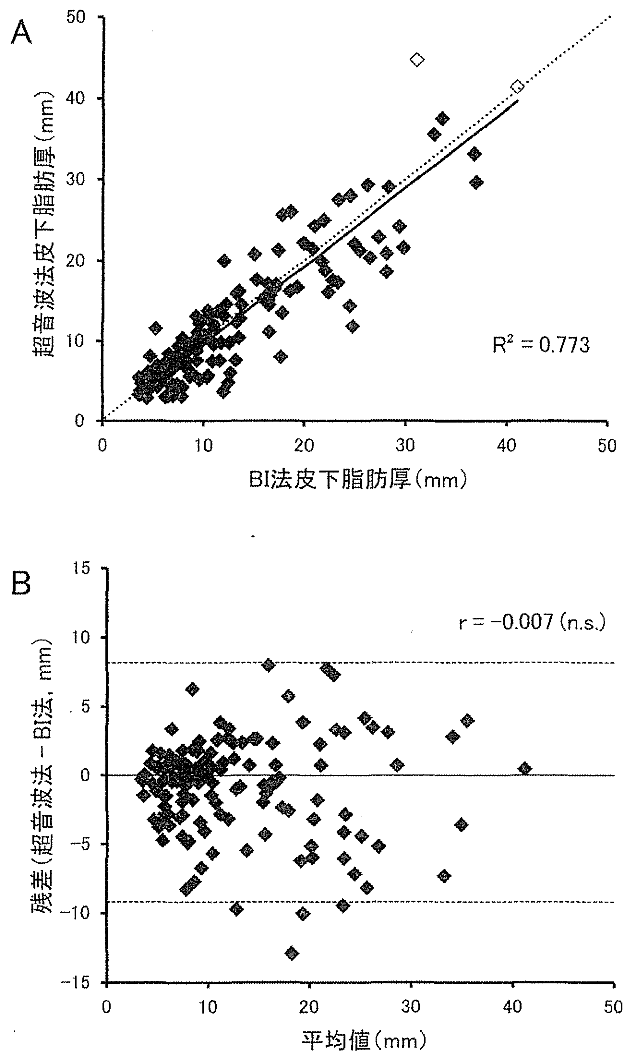

図4　グループⅡにおける推定結果
A：皮下脂肪厚の基準値と推定値との関係（点線はY＝X），B：系統誤差の確認（点線は±2SD）
なお，皮下脂肪厚が43 mm以上の箇所（図4Aにおける白抜きプロット）は，図4Bの分析から除外した．

4 B)，SEEも3.5 mmへと低下した．

考　察

本研究の主な知見は，BI法により測定したR/Xを用いることで，皮下脂肪厚が43 mm以下であれば，3.9 mmの精度で系統誤差なく推定が可能となることである．BI法による身体組成の推定において独立変数として利用されることの多いインピーダンス値は，RとXの合成，すなわち (R^2+X^2) の平方根であり，身体の中でも電気電導（伝導）性の高い水分すなわち除脂肪量を反映すると考えられてきた[9]．それに対しAckmann and Seitz[10] は，脂肪の蓄積により細胞膜や組織の電気的透過性が上昇すると，Rに比較してXが小さくなる可能性があることを示唆した．さらにBaumgartner et al.[11] は，体幹のphase angle {phase angle ＝ arctan (X/R)} が体脂肪率と有意な負の相関を示すことを報告した．Jones et al.[13] も，R，Xおよび右手－右足間の長さにより，男性30名，女性29名の体脂肪率を誤差3.2 %にて推定できたことを報告している．さらにScharfetter et al.[14] は，体脂肪率を対象とした先行研究の成果を皮下脂肪厚へと応用し，被験者数は男女12名ずつと少ないものの，インピーダンス値と腹部皮下脂肪厚との間に有意な相関が認められることを報告した．Scharfetter et al.[14] と本研究の手法に共通しているのは，電流印加電極と電圧計測電極の距離を短くし，電流を身体深部まで印加していない点である．一般に，50 kHzの周波数においては，二対の電流印加電極間の距離が長いほど組織の深部まで通電される[15]が，電流印加電極と電圧計測電極との距離が短い場合には，インピーダンス値は電極直下すなわち皮下脂肪の情報を反映する[16]．このため，本研究の予備実験においても，電極間距離を2 cm以上に伸ばすほど，皮下脂肪厚の推定精度が低くなる傾向が認められた．予備実験におけるこの結果は，電極間距離がを2 cm以上にすると皮下脂肪のみならず骨格筋まで通電され，推定誤差が生じることを示唆しているものと考えられる．一方，BI法による皮下脂肪厚推定を試みた村上と内山[17] は，見かけ比抵抗 {2π×電極間距離×(電位差／電流)} を用いて若年男性10名の大腿前部および上腕伸展部の皮下脂肪厚を推定したものの，後者における皮下脂肪厚は系統的に過大評価されたことを報告した．一般に，インピーダンス値は筋線維の走行方向[9]，組成の違い[18]や，生理周期に伴う水分分布の変化[19]などによる影響を受けやすいことから，性別・セグメント別に推定式が作成されることが多い．本研究が，村上と内山[17] とは異なり，性別や年齢に関わらず単一の推定式で身体各所の皮下脂肪を推定できたことは，本

研究の最大のメリットであるといえるであろう．一方，皮膚をつまみあげてキャリパーとよばれる皮下脂肪厚計でその厚さを測定する方法（キャリパー法）は，本研究と同様に局所の皮下脂肪厚を簡便に推定することができる唯一の手段である．しかしながら，キャリパー法測定値には皮膚が含まれる上，測定圧が高すぎると組織が圧迫されるため，この測定法による皮下脂肪厚測定値の再現性や体脂肪率との相関は低いことが，数多くの先行研究において報告されている．中でも，本研究と同様に超音波法を用いて皮下脂肪厚を測定し，キャリパー法による推定を試みたEston et al.[20]は，アジア人を対象とした場合に，両測定法による皮下脂肪厚の相関係数は0.13～0.90であり，特に上腕前部では有意な相関が認められなかったことを報告している．Eston et al.[20]と同様の分析を本研究の被験者を対象に行った場合における相関係数は0.778～0.909（いずれも$p < 0.05$）と高い値を示した．異なる被験者を対象としているため，値を直接比較することはできないものの，皮下脂肪厚の反映度としては，本研究の手法がキャリパー法を上回っていると考えられる．

本研究では，43 mm以上の皮下脂肪厚を有意に過小評価することも明らかとなった．この原因について，本研究における取得データから明らかにすることはできない．しかしながら，先述したように，50 kHzの周波数においては，電流印加電極と電圧計測電極との距離が短い場合に，インピーダンス値は電極直下の情報を反映する[14]．一方，Nagai et al.[15]が報告しているように，両電極間の距離を伸ばすことで，より身体深部の情報を反映できるようになる．仮に皮下脂肪を過大評価したのであれば，皮下脂肪以外の組織，すなわち骨格筋や内臓脂肪が測定値に影響を及ぼしている可能性が考えられるが，過小評価したという本研究の結果は，2 cmの電極間距離では，43 mm以上の深さまで通電されないことを示唆しているのかもしれない．超音波法により男性1923名，女性2416名の皮下脂肪厚を測定した安部と福永[21]によると，身体の中で皮下脂肪厚が最も高値を示すのは腹部であり，その平均値は，20～89歳の男女において最も高値を示す30代男性で19.9 ± 10.2 mm，50代女性で32.4 ± 10.9 mmである．体脂肪率が30 %以上の女性肥満者における腹部皮下脂肪厚も36.6 ± 10.4 mmであり[21]，本研究においても，腹部の皮下脂肪厚が43 mm以上となる部位を有する個人は，4名すなわち全被験者の2.8 %と少なかった．しかしながら，本研究において腹部皮下脂肪が43 mm以上となった4名のうち，一般に肥満者と定義される体格指数：30 kg/m^{2}以上であった被験者は1名のみで，他3名は，同指数が25 kg/m^{2}以下の50～60代女性であった．すなわち，中高齢女性のいわゆる「かくれ肥満」を検出できない可能性がある点は，本研究の手法を利用する際に注意が必要であろう．今後は，対象例数を増やし，皮下脂肪厚が43 mm以上の個人に対する推定精度を高めるためにさらなる検討を行う必要がある．

まとめ

本研究では，身体局所より測定したRおよびXの比を用いて皮下脂肪厚を推定する妥当性を検討した．その結果，本研究の手法により測定したR / Xを用いれば，性別，年代，部位にかかわらず，同一の回帰式によって，身体各所の皮下脂肪厚を3.5 mmの精度で推定可能であることが示唆された．その一方で，皮下脂肪厚の基準値が43 mm以上になると，皮下脂肪厚が有意に過小評価される可能性も示唆された．この点は，本研究の手法を利用するにあたり注意すべき点であると考えられた．

謝 辞

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Original Article

Use of Doubly Labeled Water to Validate a Physical Activity Questionnaire Developed for the Japanese Population

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ABSTRACT

Background: No study has attempted to use the doubly labeled water (DLW) method to validate a physical activity questionnaire administered to a Japanese population. The development and refinement of such questionnaires require that physical activity components related to physical activity level be examined.

Methods: Among 226 Japanese men and women 20 to 83 years of age, total energy expenditure (TEE) was assessed using the Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire (JALSPAQ), and the results were compared with TEE measured by the DLW method as a gold standard. Resting metabolic rate (RMR) was measured using the Douglas Bag method.

Results: The median TEE by DLW and physical activity level (PAL: TEE/RMR) were 11.21 MJ/day and 1.88, respectively, for men, and 8.42 MJ/day and 1.83 for women. JALSPAQ slightly underestimated TEE: the differences in mean and standard error were −1.15 ± 1.92 MJ/day. JALSPAQ and DLW TEE values were moderately correlated (Spearman correlation = 0.742, $P < 0.001$; intraclass correlation coefficient = 0.648, $P < 0.001$), and the 95% limit of agreement was −4.99 to 2.69 MJ. Underestimation of TEE by JALSPAQ was greater in active subjects than in less active subjects. Moderate and vigorous physical activity and physical activity during work (ie, occupational tasks and housework) were strongly related to physical activity level. However, the physical activity components that differentiated sedentary from moderately active subjects were not clear.

Conclusions: Physical activity level values on JALSPAQ and DLW were weakly correlated. In addition, estimation of TEE in active subjects should be improved, and the use of a questionnaire to differentiate activity in sedentary and moderately active subjects must be reassessed.

Key words: physical activity questionnaire; doubly labeled water; physical activity; energy expenditure

INTRODUCTION

Accurate assessment of physical activity level is fundamental in epidemiological studies that examine the effect of physical activity on disease prevention and health promotion. Although there are several methods for estimating physical activity level, questionnaires are the most common assessment tool in such studies. Many types of physical activity questionnaires are used in epidemiological studies, but a validation study of such questionnaires suggested that the reliability and validity of measurements of habitual physical activity are quite low.[1–3] In addition, Neilson et al suggested that the ability of physical activity questionnaires to predict total energy expenditure (TEE) is limited. Westerterp et al suggested that questionnaires are satisfactory as an instrument for ranking physical activity level, but not as tools for assessing absolute TEE.[4] We previously examined the International Physical Activity Questionnaire (IPAQ) and reported that it was difficult to distinguish sedentary from moderately active individuals in the Japanese population.[5] Although the IPAQ was developed for international use, we maintain that questionnaires designed to suit each country or culture would increase the validity of assessments of physical activity level. The Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire (JALSPAQ) was developed to assess physical activity in the Japan Arteriosclerosis Longitudinal Study.[6,7] This questionnaire was developed using data from physical activity records for the Japanese

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population and included detailed questions on occupational work, housework, and leisure-time physical activity.

The doubly labeled water (DLW) method is an excellent method for measuring TEE in free-living subjects over a period of 1 to 2 weeks[8] and is often used as a gold standard to validate field methods of assessing physical activity levels. However, to our knowledge, only our previous study[5] has used it to examine the validity of a questionnaire used for the Japanese population.

The primary objective of this study was to use the DLW method as the gold standard to validate a physical activity questionnaire developed for the Japanese population. To aid in the development of a valid physical activity questionnaire for Japanese, the secondary objective was to identify the physical activity component that had the greatest impact on physical activity level (PAL).

METHODS

Subjects

The study participants were 226 Japanese men and women age 20 to 83 years (mean ± standard deviation, 50.4 ± 17.1 years) who volunteered at community health care centers and workplaces or enrolled via the internet homepage of our institute. The inclusion criteria of the present study were as follows: absence of any condition affecting energy or water metabolism (eg, thyroid or kidney disease), not pregnant or breast-feeding, residence in home prefecture 2 weeks before and during the study, not on weight-loss or treatment diet, and not consuming more than 40 grams of alcohol per day. The occupations of the participants were homemaker ($n = 59$), office worker ($n = 57$), shipbuilder ($n = 17$), shop assistant ($n = 14$), no regular work ($n = 14$), nurse ($n = 13$), teacher ($n = 11$), salesperson ($n = 11$), factory worker ($n = 6$), clinical examination technician ($n = 5$), physiotherapist ($n = 4$), and other ($n = 12$, cleaner, gardener, dietitian, priest, sports instructor, carpenter, etc.). We were unable to randomly select subjects according to physical activity level. Over the entire assessment period, the participants were carefully instructed to maintain their normal daily activities and eating patterns and to make no conscious effort to lose or gain weight.

Study protocol

This study was approved by the Ethics Committee of the National Institute of Health and Nutrition in Japan. All subjects gave their informed consent in writing before the investigation was begun. TEE was estimated over 1 or 2 weeks, depending on the 2 half-lives of the isotopes used in the DLW method. Body mass and height were measured in the fasting state before administering the dose of DLW and on the last day of the study. On the first day of the study period, baseline urine was collected, and measurements of resting metabolic rate (RMR) and DLW dosing were obtained. The physical activity questionnaire and dietary assessment were completed between the 10th and 12th day of the study period and were checked by the researchers on the last day.

Measurement of resting metabolic rate

Subjects were instructed to refrain from moderate to vigorous physical activity for 24 hours, to fast at least 12 hours, and to get sufficient sleep before the measurements. They were instructed to arrive at the laboratory between 8AM and 9AM. After arrival, they rested quietly in the supine position for 30 minutes before the measurements. Using a mask connected to a Douglas bag, expired gas was collected twice for 10 minutes, with a 1-minute interval between collections. During all RMR measurements, the room temperature was maintained at approximately 24°C. Subjects were lying down and fully awake during the measurements. They were also free from emotional stress and were familiar with the apparatus used. The volume of expired air was measured with a certified gas meter (DC-5, Shinagawa, Tokyo, Japan), the accuracy and precision of which were maintained within 1% of the coefficient of variation (CV). Concentrations of oxygen and carbon dioxide were measured with a mass spectrometer (ARCO-1000, Arco Systems, Chiba, Japan). The precision of expired gas measurement was 0.02% for oxygen and 0.06% for carbon dioxide. RMR was calculated using Weir's equation.[9]

DLW energy measurement

After providing a baseline urine sample, a single dose of approximately 0.06 g/kg body weight of $^{2}H_2O$ (99.8 atom%, Cambridge Isotope Laboratories, MA, USA) and 1.4 g/kg body weight of $H_2{}^{18}O$ (10.0 atom%, Taiyo Nippon Sanso, Tokyo, Japan) was given orally to each subject. Then subjects were asked to collect urine samples at 8 predetermined times during the study period, at the same time of day. Except for the baseline collection, all urine samples were collected by the participant, and the time of sampling was recorded. All samples were stored by freezing at −30°C in airtight parafilm-wrapped containers and then analyzed in our laboratory.

Gas samples for the isotope ratio mass spectrometer (IRMS) were prepared by equilibration of the urine sample with a gas. CO_2 was used to equilibrate ^{18}O, and H_2 was used for ^{2}H. Pt catalyst was used for equilibration of ^{2}H. The gas sample of the CO_2 and H_2 was analyzed by IRMS (DELTA Plus; Thermo Electron Corporation, Bremen, Germany). Each sample and the corresponding reference were analyzed in duplicate. The average standard deviations for the analyses were 0.5‰ for ^{2}H and 0.03‰ for ^{18}O. TEE was expressed as mean TEE per day over the study period.

Calculations of isotopic abundance and TEE

The ^{2}H and ^{18}O zero-time intercepts and elimination rates (k_H and k_O) were calculated using a least-squares linear regression on the natural logarithm of isotope concentration as a function of the elapsed time from dose administration. Zero-time intercepts were used to determine the isotope pool sizes. Total body water (TBW) was calculated from the mean value of the isotope pool size of ^{2}H divided by 1.041 and that of ^{18}O divided by 1.007. The mean ko/kd of the present study was 1.28 ± 0.06 (range, 1.15–1.56). All ko/kd values were maintained within the recommended range (1.1 to 1.7) for quality control of the analysis, as recommended by the International Atomic Energy Agency.[10] rCO_2 was calculated as follows: $rCO_2 = 0.4554 \times TBW \times (1.007ko - 1.041k_H)$. Calculation of TEE (kcal/day) was performed using a modified Weir's formula based on the CO_2 production rate (rCO_2) and food quotient (FQ).[9] FQ was calculated from the dietary survey during the study period. The calculation assumed that under conditions of perfect nutrient balance, the FQ must equal the respiratory quotient (RQ).[11–13] The average FQ of each occupational group was used for each group (FQ = 0.85–0.95). However, FQ values stratified by occupational group, sex, and age were not significantly different. Physical activity level (PAL) was calculated as TEE/RMR.

Physical activity questionnaire

The physical activity questionnaire developed for the Japan Arteriosclerosis Longitudinal Study (JALSPAQ) was used in this study.[6,7] This questionnaire comprises 14 questions on occupation, locomotion, housework, sleep time, and leisure-time physical activities. In this questionnaire, occupational work was assessed as duration of sitting, standing, walking, and heavy work. Heavy work was defined as lifting more than 10 kg or manual labor of similar intensity. Leisure-time physical activity was assessed by type, duration, and frequency. Questionnaire data were converted to the intensity of each physical activity expressed in metabolic equivalents (METs), according to the Compendium by Ainsworth et al, and summarized as METs·h/day and energy expenditure.[14] In the present study, we used TEE per day, METs·h/day, and PAL as indices of physical activity level from JALSPAQ. Duration of light (<3 METs), moderate (3–5.9 METs), and vigorous (≥6 METs) physical activities was calculated for all physical activities (including occupational activity, housework, and leisure-time physical activity), as well as for leisure-time physical activity only. Working time, including occupational and housework time, was divided into the duration of sitting (<2 METs), standing (2 to <3 METs), walking (3 to <6 METs), and heavy work (≥6 METs), including housework. We calculated the durations of occupational activity and housework together because their frequencies and durations were quite complicated.

Dietary assessment

Dietary habits were assessed by using a brief self-administered diet history questionnaire (BDHQ)—a 4-page structured questionnaire that requested information on the consumption frequencies for a total of 56 food and beverage items, with specified serving sizes described in terms of the servings commonly consumed in the general Japanese population.[15] Energy and macronutrient intakes were calculated using a computer algorithm for the BDHQ, which was based on the Standard Tables of Food Composition in Japan. FQ was calculated by using the equation of Black et al.[11]

Statistical analysis

Statistical analyses were performed using SPSS for Windows (version 16.0J; SPSS Inc., IL, USA). Physical characteristics are classified using the sex and age groups outlined in the Dietary Reference Intake (DRI) of Japan. The estimated energy expenditure data were generally not normally distributed; therefore, medians and interquartile ranges are used to describe these results. Sex and age-group differences were compared using 2-way analysis of covariance. The Bonferroni procedure was used as the post-hoc test. The relation between TEE as estimated by DLW and JALSPAQ was expressed as Spearman correlations, intraclass correlation coefficient (ICC), and 95% limits of agreement (95% LOA: mean difference $\pm 2 \times$ SD of the mean difference). Bland-Altman plots were also created to evaluate the differences between the 2 methods. To examine the type of physical activities that affected physical activity level, we used 1-way analysis of covariance, Pearson's correlation coefficients, and partial correlation coefficients adjusted for sex and age group.

RESULTS

The physical characteristics of the subjects are shown in Table 1. Body weight did not change significantly during the study period ($P = 0.313$). Among all subjects, 2.8% of men and 6.8% of women were classified as lean (body mass index [BMI] <18.5 kg/m^2), and 31.5% of men and 17.8% of women were classified as obese (BMI >25 kg/m^2) according to the criteria for Japanese.[16] The average TBW was 37.3 ± 7.1 kg in men and 25.9 ± 2.8 kg in women. When 73.2% was defined as the proportion of water in fat-free mass, the percent of fat mass was $24.3 \pm 6.1\%$ in men and $33.4 \pm 7.0\%$ in women.[17] Three men aged 30 to 49 years had a body weight higher than 100 kg; however, they were fit and their percent of fat mass was less than 25%. In addition, in the assessment of TEE by DLW and JALSPAQ, they did not significantly differ from other subjects.

The medians plus interquartiles for RMR, TEE, and PAL by DLW, TEE by questionnaire, and the differences between the 2 methods are shown by sex and age group in Table 2. The respective medians of TEE and PAL were 11.21 MJ/day and 1.88 for men and 8.42 MJ/day and 1.83 for women. PAL significantly differed by age group, but not by sex. PAL in subjects older than 70 years was significantly higher than in those aged 30 to 49 years ($P = 0.016$) and 50 to 69 years

Table 1. Characteristics of study subjects

Age group, years	n	Age (years)	Height (cm)	Body weight pre (kg)	Body weight post (kg)	Body weight change (kg)	BMI (kg/m^2)	TBW (kg)
Male								
20–29	18	25.0 ± 2.5	171.5 ± 6.0	62.1 ± 7.9	62.3 ± 8.0	0.2 ± 0.7	21.1 ± 2.0	36.4 ± 3.7
30–49	42	36.7 ± 5.3	173.8 ± 6.6	74.8 ± 16.7	74.9 ± 16.6	0.0 ± 1.1	24.6 ± 4.7	41.8 ± 8.3
50–69	31	60.2 ± 6.5	163.8 ± 6.6	63.9 ± 8.1	64.0 ± 8.3	0.1 ± 0.9	23.8 ± 2.4	34.5 ± 4.1
≥70	17	75.1 ± 4.0	162.1 ± 5.0	60.7 ± 8.1	60.8 ± 8.2	0.2 ± 0.9	23.1 ± 2.7	32.0 ± 4.2
Female								
20–29	8	25.3 ± 2.4	157.0 ± 3.9	51.3 ± 2.5	51.2 ± 2.5	−0.1 ± 0.8	20.9 ± 1.6	25.5 ± 1.5
30–49	42	38.7 ± 4.4	158.0 ± 5.4	53.7 ± 8.3	53.7 ± 8.3	0.0 ± 0.7	21.5 ± 3.2	26.9 ± 3.1
50–69	49	62.0 ± 5.1	154.0 ± 4.6	54.6 ± 7.8	54.7 ± 7.9	0.1 ± 0.7	23.0 ± 3.2	25.8 ± 2.7
≥70	19	73.4 ± 3.9	148.0 ± 4.4	50.2 ± 6.1	50.1 ± 6.1	0.1 ± 0.6	22.9 ± 2.8	24.1 ± 2.0

All values are mean ± SD, unless otherwise indicated.
BMI: body mass index; TBW: total body water measured by doubly labeled water method.

Table 2. Resting metabolic rate (RMR) and total energy expenditure (TEE) measured by doubly labeled water (DLW) method and questionnaire

Age group, years		RMR (MJ/day)	TEE by DLW (MJ/day)	PAL	TEE by JALSPAQ (MJ/day)	Difference between DLW and JALSPAQ (MJ/day)	Difference between DLW and JALSPAQ (%)
Male							
	20–29	6.27 (0.92)	12.00 (0.19)	1.89 (0.35)	9.60 (2.12)	−1.69 (2.89)	−15.7 (23.0)
	30–49	6.72 (1.53)	12.88 (4.64)	1.87 (0.45)	11.14 (2.85)	−1.18 (3.30)	−9.5 (20.3)
	50–69	5.50 (1.30)	10.81 (2.11)	2.08 (0.55)	9.18 (1.61)	−2.02 (1.99)	−18.1 (17.5)
	≥70	5.76 (1.41)	11.76 (3.59)	2.11 (0.52)	8.03 (1.65)	−0.97 (2.34)	−12.2 (21.0)
Female							
	20–29	4.73 (0.27)	8.10 (1.18)	1.86 (0.22)	7.43 (1.01)	−1.09 (1.85)	−13.2 (22.3)
	30–49	4.83 (0.82)	8.82 (1.80)	1.84 (0.32)	7.33 (1.75)	−1.26 (1.73)	−14.9 (19.1)
	50–69	4.58 (0.95)	8.53 (1.42)	1.86 (0.37)	8.12 (1.28)	−0.43 (1.76)	−5.3 (20.4)
	≥70	4.62 (0.99)	8.56 (0.86)	1.86 (0.41)	7.08 (1.33)	−0.36 (1.68)	−5.2 (23.3)
P value	Sex	<0.001	<0.001	0.067	<0.001	0.003	0.071
	Age group	<0.001	<0.001	<0.001	<0.001	0.335	0.370
	Sex by age	0.010	0.004	0.481	<0.001	0.591	0.188

All values are median (interquartile), unless otherwise indicated.
PAL: physical activity level (TEE/RMR); JALSPAQ: Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire.

($P < 0.001$). JALSPAQ slightly underestimated TEE, with differences in mean and standard error of the mean of −1.15 ± 1.92 MJ/day and −0.020 ± 0.030 MJ/kg/day. TEE values by JALSPAQ and DLW were moderately correlated (Spearman correlation = 0.742, $P < 0.001$; ICC = 0.648, $P < 0.001$). The 95% LOA was −4.99 to 2.69 MJ. The absolute difference between TEE values by DLW and JALSPAQ was significantly greater in men than in women, but the percent difference was not significantly different. The Spearman correlation coefficient and ICC for PAL were 0.423 ($P < 0.001$) and 0.332 ($P < 0.001$), respectively, and the 95% LOA for PAL was −0.86 to 0.46. Use of Bland-Altman plots to compare TEE and PAL by DLW and JALSPAQ suggested that TEE tended to be underestimated in subjects with higher TEE (Spearman correlation, −0.201; $P = 0.002$); however, most values were within the 2 SD of the difference in TEE as determined by the 2 methods (Figure). PAL was not underestimated even in subjects with higher PALs (Spearman correlation, −0.011; $P = 0.866$); however, individual differences were widely distributed.

Using PAL determined using TEE measured by DLW, the subjects were divided into 3 groups according to Dietary Reference Intake (Table 3).[18] The proportions of active (PAL >1.9), moderately active (PAL 1.6 to <1.9), and sedentary (PAL <1.6) individuals were 45.4%, 43.5%, and 11.1% in men, respectively, and 40.7%, 41.5%, and 17.8% in women. TEE by JALSPAQ in the sedentary group was significantly lower than in moderately active and active adults. Total METs assessed by JALSPAQ was lower in sedentary and moderately active individuals than in active individuals. The differences between the 2 methods in the TEE of sedentary and moderately active adults were significantly smaller than in active adults. The total duration of each intensity of physical activity, including occupational and housework activity and leisure-time physical activity, was compared among physical activity levels. The duration of moderate and vigorous

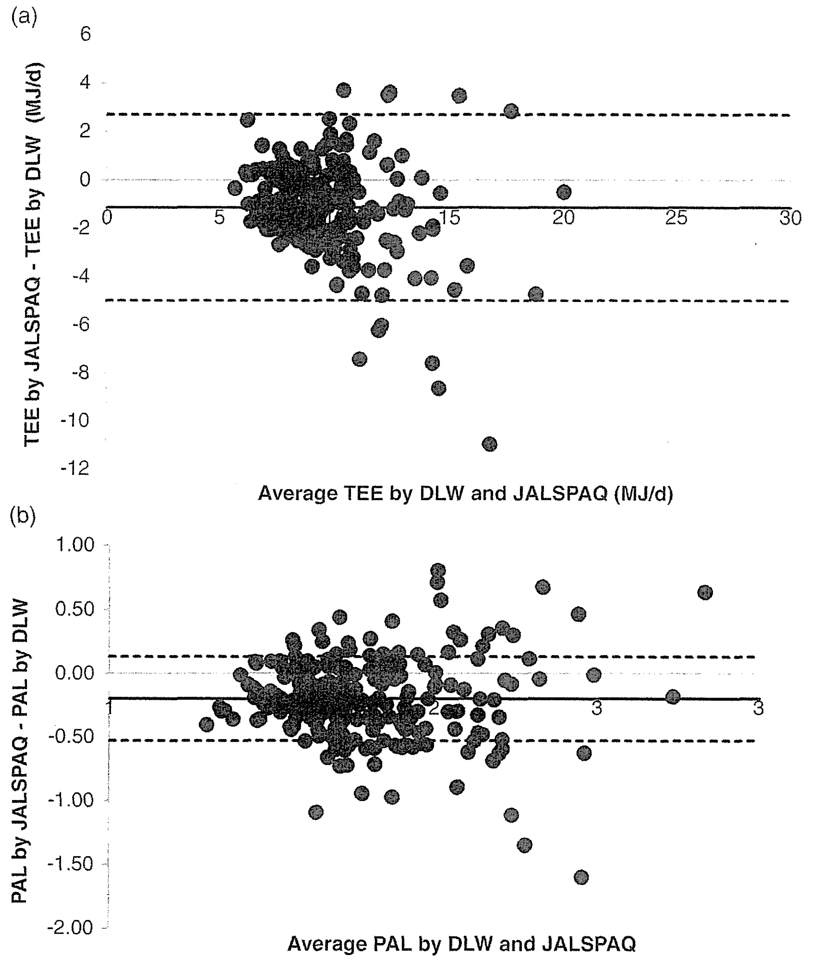

Figure. Bland-Altman plots of total energy expenditure (TEE) and physical activity level (PAL). (a) Comparison of mean TEE estimated by the doubly labeled water (DLW) method and the Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire (JALSPAQ), and the difference in TEE as estimated by the 2 methods. (b) Comparison of mean PAL by DLW and JALSPAQ, and the difference in PAL as estimated by the 2 methods. Solid lines indicate the mean difference, and the broken lines indicate 2 SD limits.

physical activity in sedentary and moderately active adults was significantly shorter than in active adults. When we compared only leisure-time physical activity, there was no difference in duration of physical activity. Regarding physical activity during work, duration of walking was significantly shorter in sedentary individuals than in moderately active and active individuals. In addition, walking duration was significantly shorter in moderately active adults than in active adults. The proportion of heavy work differed significantly among groups; greater activity was associated with heavier work.

Regarding the types of physical activity that were correlated with PAL, correlation coefficients and partial correlation coefficients adjusted for sex and age group are shown in Table 4. Duration of total, moderate, and vigorous physical activity were weakly correlated with PAL. However, duration of leisure-time physical activity was not correlated with PAL. During working time, duration of standing, walking, and heavy work were weakly correlated with PAL.

DISCUSSION

This study used the DLW method as a gold standard to examine the validity of a physical activity questionnaire designed for the Japanese population in a large number of subjects with widely varying physical activity levels. With the DLW method as the gold standard, JALSPAQ estimated TEE relatively well, but underestimation was more frequent at higher physical activity levels.

The body height and weight of the present subjects were similar to the standard values for the Japanese population.[18] RMR was also similar to the standard RMR values for the Japanese population presented in Dietary Reference Intake.[18] Thus, we conclude that the present subjects had the general physical characteristics of the Japanese general population. However, the physical activity level of the present subjects was higher than that noted in our previous studies: 42.9% of the present subjects were classified as active, using the definition in the Dietary Reference Intake.[18] We recruited

Table 3. Total energy expenditure (TEE) and duration of each activity among groups by physical activity level

	Physical activity level			*P*
	I Sedentary	II Moderately active	III Active	
TEE by DLW (MJ/day)	8.11 (1.39)[a,b]	9.18 (2.29)[b]	10.76 (4.25)	*<0.001*
TEE by questionnaire (MJ/day)	7.78 (1.21)[b,c]	8.45 (2.87)	8.90 (3.06)	0.006
Total METs (METs·h/day)	33.5 (4.1)[b]	34.4 (4.8)[b]	35.8 (6.4)	<0.001
Difference in TEE between DLW and PAQ (MJ/day)	−0.07 (0.50)[b]	−0.80 (1.62)[b]	−2.02 (2.23)	<0.001
Difference in TEE between DLW and PAQ (%)	−0.9 (15.3)[b]	−8.4 (17.6)[b]	−19.1 (19.0)	<0.001
Total duration of physical activity (h/day)				
Light (<3 METs)	3.41 (3.58)	4.14 (3.50)	4.16 (3.72)	0.155
Moderate (3–5.9 METs)	1.65 (1.81)[b]	2.06 (2.07)[b]	2.53 (3.89)	<0.001
Vigorous (≥6 METs)	0.00 (0.09)[b]	0.00 (0.20)[a]	0.0 (0.54)	0.007
Duration of leisure-time physical activity (h/day)				
Light (<3 METs)	0.00 (0.26)	0.00 (0.07)	0.00 (0.09)	0.766
Moderate (3–5.9 METs)	0.01 (0.17)	0.02 (0.23)	0.03 (0.27)	0.965
Vigorous (≥6 METs)	0.00 (0.08)	0.00 (0.02)	0.00 (0.00)	0.556
Duration of work (h/day)				
Sitting	0.00 (2.86)	1.55 (4.61)	0.00 (4.29)	0.129
Standing	1.75 (2.20)	1.42 (2.14)	2.00 (2.85)	0.176
Walking	0.25 (0.86)[b,c]	0.54 (1.90)[b]	1.00 (3.07)	<0.001
Proportion of subjects participating in heavy work (%)	6.1	24	36.1	0.003

TEE: total energy expenditure; DLW: doubly labeled water; MET: metabolic equivalent; PAQ: physical activity questionnaire.
All values are median (interquartile), unless otherwise indicated.
[a]$P < 0.05$ as compared with physical activity level III.
[b]$P < 0.01$ as compared with physical activity level III.
[c]$P < 0.01$ as compared with physical activity level II.

Table 4. Correlation coefficients for physical activity level (as measured by doubly labeled water method) and duration of physical activities

	Correlation coefficient	*P* value	Partial correlation coefficient	*P* value
Total duration of physical activity (h/day)				
Light (<3 METs)	0.034	0.608	0.022	0.746
Moderate (3–5.9 METs)	0.257	<0.001	0.225	0.001
Vigorous (≥6 METs)	0.354	0.481	0.330	<0.001
Duration of leisure-time physical activity (h/day)				
Light (<3 METs)	−0.018	0.790	0.008	0.910
Moderate (3–5.9 METs)	0.002	0.978	0.000	0.996
Vigorous (≥6 METs)	−0.048	0.474	−0.072	0.286
Duration of work (h/day)				
Sitting	−0.064	0.337	−0.133	0.047
Standing	0.165	0.013	0.256	<0.001
Walking	0.271	<0.001	0.239	<0.001
Heavy	0.376	<0.001	0.354	<0.001

MET: metabolic equivalent; TEE: total energy expenditure.
Partial correlation coefficients are adjusted for sex and age group.

subjects at worksites requiring vigorous physical activity (ie, shipbuilding and hospitals). This may explain the higher physical activity level of the subjects.

Neilson et al reviewed a validation study of a physical activity questionnaire and suggested that, at the group level, the mean difference in TEE ranged from −800 to 1589 kcal/day (−3.35 to 6.65 MJ/day) and that the Spearman correlation coefficient for TEE ranged from 0.15 to 0.51.[2] As compared with these results, JALSPAQ showed a smaller negative mean difference of −1.15 MJ/day and a higher correlation (Spearman correlation, 0.742; $P < 0.001$). A comparison of individual-level agreement indicates that the width of the 95% LOA in our study (7.68 MJ/day) was smaller than that in most other questionnaires described in the review of Neilson and colleagues (1133 to 17 948 kcal/day; 4.74 to 75.09 MJ/day).[2] The relatively good agreement in this study partly resulted from the greater number of subjects ($n = 226$ in the present study vs $n = 13$ to $n = 65$ in previous studies) and the wide variation in TEE. Standard deviation was 2.77 MJ in the present study and 0.35 to 3.51 MJ in previous studies. A study by Racette showed the lowest 95% LOA (−2.42 to 0.16 MJ/day).[19] However, that study was part of an investigation of a 17-week outpatient weight loss treatment, so the subjects were thought to be highly motivated and to have answered the questionnaire carefully. One reason why TEE is assumed to have greater accuracy than the existing questionnaire is that it is believed to have more detailed questions regarding occupational activity, housework, and leisure-time physical activity.

JALSPAQ tended to greatly underestimate TEE in more active subjects, possibly because the algorithm for the calculation of TEE for JALSPAQ only includes duration of time spent sitting, standing, and walking. These activities were scored on a scale from 1.5 to 4.0 METs. Even when there was a question regarding carrying heavy objects or engaging in activity of similar intensity, such activity was not used to calculate TEE. Thus, underestimation would be greater in subjects who expended considerable energy at work. In the present study, 16 subjects were engaged in shipbuilding, and the differences between TEE by DLW and JALSPAQ ranged from −10.98 to 0.34 MJ/day; TEE was overestimated by JALSPAQ in only 2 subjects.

Although TEE estimated by JALSPAQ showed a relatively good correlation with TEE by DLW, RMR accounted for a large part of TEE. To lessen the contribution of RMR, PAL was compared between the two methods. The results for PAL were poor, and individual differences were widely distributed. Therefore, JALSPAQ must either be improved or another new questionnaire should be developed to assess individual PAL.

We also attempted to identify a physical activity that characterized physical activity level. Our results showed that total time spent in moderate physical activity was significantly greater in the active group. In addition, moderate and vigorous physical activity had a weak but significant correlation with PAL. Thus, moderate physical activity is an important component of physical activity level, as Westerterp has suggested.[20] However, the duration of moderate physical activity did not differ in the sedentary and moderate groups. Wareham et al used a very brief questionnaire that only included physical activity during work and recreational activities and found that physical activity ratio (daytime energy expenditure/resting metabolic rate), which was estimated using a heart rate monitor, did not differ between inactive and moderately inactive groups, even though VO_{2max} was different between these groups.[21] Another method of classifying physical activity in sedentary subjects should thus be considered.

The present results also suggest that intensity and duration of physical activity during work (including occupational activity and housework) strongly affect PAL, whereas leisure-time physical activity does not. Both work and leisure-time physical activity play fundamental roles in total physical activity, which explains why previous brief physical activity questionnaires assessed only physical activity during work and leisure time.[21,22] In the present study, because the mean duration of all leisure-time physical activity was 22 ± 21 minutes per day, the effect of leisure-time physical activity on TEE might be very small.

The most significant limitation of this study was that subjects were not selected randomly: they joined the study as volunteers. Hence, as compared with the general population, they might have remembered their physical activities better and completed the questionnaire more carefully. In addition, the variation in their physical activity level might differ from that of the general Japanese population. However, we were unable not determine the nature or extent of error that resulted from these subject characteristics. A second limitation is that the study periods for DLW and JALSPAQ were not identical. The DLW method determined the average TEE over 1 or 2 weeks. In contrast, JALSPAQ assessed typical physical activity over 1 month. This discrepancy could affect the validation of JALSPAQ. Finally, the relatively small proportion of sedentary subjects made it difficult to characterize the sedentary population. Although we tried to collect subjects with a broad range of physical activities, we could not collect comparable numbers of sedentary and active subjects.

In conclusion, PAL by JALSPAQ weakly correlated with PAL by DLW, although TEE by JALSPAQ was better correlated with TEE by DLW than with TEE assessed by the questionnaires used in previous studies. TEE underestimation was greater in active subjects than in sedentary and moderately active subjects. In addition, in this population, total moderate physical activity and physical activity during work were related to physical activity level, whereas leisure-time physical activity was not. To improve the physical activity questionnaire, an algorithm for heavy work should be added. In addition, to better differentiate sedentary subjects form moderate subjects, additional questionnaire items should be added or the algorithm should be reevaluated.

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SHORT COMMUNICATION

Relation between cigarette smoking and ventilatory threshold in the Japanese

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Abstract The link between cigarette smoking and ventilatory threshold (VT) was investigated. We used data for 407 men and 418 women not taking medication. Habits of cigarette smoking were obtained through interviews by well-trained staff. The influence of cigarette smoking on oxygen uptake, work rate, and heart rate at VT was evaluated. Oxygen uptake at VT in women and work rate at VT in men with cigarette smoking were significantly lower than in subjects without cigarette smoking after adjusting for age. The differences of parameters at VT did not reach significant levels after adjusting for age and exercise habits in both sexes. However, in women without exercise habits, there was significant difference of oxygen uptake at VT between women with and without cigarette smoking after adjusting for age [cigarette smoking (+): 11.5 ± 1.8 ml/kg/min, cigarette smoking (−): 12.4 ± 2.1 ml/kg/min, $p = 0.0006$]. The number of cigarettes smoked per day and the Brinkman Index were not clearly correlated with oxygen uptake at VT. A combination of promoting exercise habits and prohibiting cigarette smoking might be recommended for improving the aerobic exercise level, especially in women.

Keywords Cigarette smoking · Ventilatory threshold · Oxygen uptake · Exercise habits

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Introduction

Cigarette smoking has become an important public health challenge, and it has been reported that 39.4% of men and 11.0% of women are current smokers in Japan [1]. Cigarette smoking is also a strong risk factor for atherosclerosis and cardiovascular disease in a dose-dependent manner [2].

Exercise is considered as a useful method for preventing and improving atherosclerosis and cardiovascular disease. The ventilatory threshold (VT) is defined as the upper limit of aerobic exercise and is thought to serve as an accurate and reliable standard for exercise prescription [3]. Since the exercise intensity at VT is not harmful to cardiovascular function, it can be safely applied to patients with myocardial infarction as an exercise prescription [4]. We have previously reported that aerobic exercise level was significantly lower in subjects with metabolic syndrome than that in subjects without the syndrome [5], and the prevalence of metabolic syndrome was significantly higher in subjects with cigarette smoking than that in subjects without cigarette smoking [6]. However, the relationship between cigarette smoking and aerobic exercise level defined by VT is not fully discussed.

The aim of this study is to explore the link between cigarette smoking and VT in the Japanese population.

Subjects and methods

Subjects

We used data for 407 Japanese men (aged 42.1 ± 11.4 years) and 418 women (aged 44.8 ± 12.0 years) (5.8%), retrospectively from a database of 14,345 subjects who met the following criteria: they had (1) wanted to change their lifestyle, i.e., diet and exercise habits, and had received an annual health checkup from June 1997 to May 2007 at Okayama Southern Institute of Health, (2) they had received anthropometric and oxygen uptake at VT measurements and evaluation of cigarette smoking as part of the annual health checkup, (3) received no medications for diabetes, hypertension, and/or dyslipidemia, and (4) provided written informed consent (Table 1).

Ethical approval for the study was obtained from the Ethical Committee of Okayama Health Foundation.

Anthropometric measurements

Anthropometric and body compositions were evaluated based on the following parameters: height, body weight, abdominal circumference, and hip circumference. Abdominal circumference was measured at the umbilical level, and the hip was measured at the widest circumference over the trochanter in standing subjects after normal exhalation [7].

Cigarette smoking

The data on cigarette smoking were obtained at interviews by well-trained staff in a structured way. The subjects were asked if they currently smoked cigarettes. When the answer was "yes," they were classified as current smokers and further questions were asked regarding the average number of cigarettes smoked per day and their age at starting smoking. When the answer was "no," they were classified as nonsmokers.

Based on answers to those questions, the cumulative amount of cigarette consumption expressed as the Brinkman Index (BI: number of cigarettes consumed per day multiplied by years of smoking) [8].

Table 1 Clinical profiles of enrolled subjects

	Mean ± SD	
	Men	Women
Number of subjects	407	418
Age (years)	42.1 ± 11.4	44.8 ± 12.0
Height (cm)	169.9 ± 5.8	156.0 ± 5.5
Body weight (kg)	79.1 ± 13.3	65.0 ± 12.9
Abdominal circumference (cm)	91.1 ± 10.9	81.4 ± 11.2
Hip circumference (cm)	98.6 ± 6.8	96.7 ± 8.5
Oxygen uptake at ventilatory threshold (ml/kg/min)	14.9 ± 3.9	12.6 ± 2.5
Work rate at ventilatory threshold (W)	82.9 ± 24.4	51.3 ± 14.6
Heart rate at ventilatory threshold (beats/min)	106.0 ± 11.9	107.0 ± 11.8

Exercise testing

A graded ergometer exercise protocol [9] was performed. Two hours after breakfast, a resting electrocardiogram (ECG) was recorded and blood pressure was measured. Then, all participants were given graded exercise after 3 min of pedaling on a bicycle ergometer at zero load (Excalibur V2.0; Lode BV, Groningen, The Netherlands). The profile of incremental workloads was automatically defined using the methods of Jones et al. [9], in which the workloads reach the predicted $\dot{V}O_{2\,max}$ in 10 min. A pedaling cycle rate of 60 rpm was maintained. Loading was terminated when the appearance of symptoms forced the subject to stop. During the test, ECG was monitored continuously together with recording of heart rate (HR). Exhaled gas was collected, and rates of oxygen consumption $\dot{V}O_2$ and carbon dioxide production ($\dot{V}CO_2$) were measured breath by breath using a cardiopulmonary gas exchange system (Oxycon Alpha; Mijnhrdt b.v., The Netherlands). VT was determined by the standard of Wasserman et al. [3], Davis et al. [10], and the V-slope method of Beaver [11] from $\dot{V}O_2$, $\dot{V}CO_2$, and minute ventilation ($\dot{V}E$). At VT, $\dot{V}CO_2$ (ml/kg/min), work rate (W), and heart rate (beats/min) were measured and recorded.

Exercise habits

The data on exercise habits were obtained through interviews by well-trained staff in a structured way according to the National Nutrition Survey in Japan [12]. The subjects were asked if they currently exercise (over the level of 30 min per session, two times per week, and prolonged duration for 3 months). When the answer was "yes," they were classified as subjects with exercise habits. When the answer was "no," they were classified as subjects without exercise habits.

Statistical analysis

All data are expressed as mean ± standard deviation (SD). Statistical analysis was performed using an unpaired t test, χ^2 test, logistic regression analysis, covariance analysis, one-way analysis of variance (ANOVA), and Scheffè's *F* test, where $p < 0.05$ was considered to be statistically significant. We used the unpaired *t* test to compare parameters between subjects with and without cigarette smoking; the χ^2 test was used to evaluate the relationship between cigarette smoking and exercise habits. Logistic regression analysis and covariance analysis were also used to adjust for parameters. ANOVA and Scheffe's *F* test were used to compare among subjects with and without cigarette smoking and exercise habits. Pearson's correlation coefficients were calculated and used to test the significance of the linear relationship between oxygen uptake at VT and the number of cigarette smoked per day, the BI.

Results

The results of age and parameters at VT in subjects with and without cigarette smoking are presented in Table 2. A total of 166 men (40.8%) and 46 women (11.0%) were current smokers. In men, there was no significant difference of age between subjects with and without cigarette smoking. Oxygen uptake and work rate at VT in subjects with cigarette smoking were significantly lower than those in subjects without cigarette smoking. However, in women, age in subjects with cigarette smoking was significantly lower than that in subjects without cigarette smoking. Therefore, to avoid the influence of age on parameters at VT, we used age as a covariate and compared parameters at VT using covariance analysis. Oxygen uptake in women and work rate at VT in men with cigarette smoking were significantly lower than in subjects without cigarette smoking even after adjusting for age (Table 2).

It is well known that aerobic exercise level is closely linked to exercise habits [5]. We evaluated the relationship between cigarette smoking and exercise habits (Table 3). A total of 164 men (40.3%) and 105 women (25.1%) were defined as having exercise habits. In men, the prevalence of subjects with cigarette smoking was significantly lower in subjects with exercise habits than that in subjects without exercise habits (Table 3). However, no significant difference in the prevalence of cigarette smoking in subjects with and without exercise habits was noted in women.

To avoid the influence of age and exercise habits on cigarette smoking, we used age, exercise habits, and parameters of VT as explanatory variables, and cigarette smoking as a response variable. No significant differences of parameters at VT in subjects with and without cigarette

Table 2 Comparison of parameters at ventilatory threshold between subjects with and without cigarette smoking

	Mean ± SD		*p*	*p* (after adjusting for age)	*p* (after adjusting for age and exercise habits)
	Cigarette smoking (+)	Cigarette smoking (−)			
Men					
Number of subjects	166	241			
Age (years)	41.8 ± 11.0	42.4 ± 11.7	0.5803		
Oxygen uptake at ventilatory threshold (ml/kg/min)	14.3 ± 3.1	15.3 ± 4.4	**0.0193**	0.0595	0.1156
Work rate at ventilatory threshold (W)	79.8 ± 20.7	85.0 ± 26.5	**0.0333**	**0.0377**	0.0764
Heart rate at ventilatory threshold (beats/min)	105.5 ± 11.0	106.3 ± 12.5	0.4683	0.9970	0.1839
Women					
Number of subjects	46	372			
Age (years)	39.6 ± 12.9	45.4 ± 11.8	**0.0019**		
Oxygen uptake at ventilatory threshold (ml/kg/min)	12.0 ± 2.8	12.7 ± 2.4	0.1011	**0.0120**	0.0514
Work rate at ventilatory threshold (W)	52.9 ± 18.1	51.1 ± 14.1	0.4092	0.6883	0.6414
Heart rate at ventilatory threshold (beats/min)	106.2 ± 11.4	107.1 ± 11.9	0.6136	0.2680	0.0881

Table 3 Relationship between cigarette smoking and exercise habits

	Exercise habits (+)	Exercise habits (−)	*p*	*p* (after adjusting for age)
Men				
Cigarette smoking (+)	52	114	**0.0022**	**0.0024**
Cigarette smoking (−)	112	129		
Women				
Cigarette smoking (+)	8	38	0.2002	0.5304
Cigarette smoking (−)	97	275		

smoking were noted after adjusting for age and exercise habits in both sexes (Table 2). We separately compared oxygen uptake at VT in subjects without exercise habits. After adjusting for age, no significant difference of oxygen uptake at VT was noted between men with and without cigarette smoking [cigarette smoking (+): 13.8 ± 2.6 ml/kg/min, cigarette smoking (−): 13.8 ± 2.5 ml/kg/min, $p = 0.4089$]. However, there was significant difference of oxygen uptake at VT between women with and without cigarette smoking [cigarette smoking (+): 11.5 ± 1.8 ml/kg/min, cigarette smoking (−): 12.4 ± 2.1 ml/kg/min, $p = 0.0006$].

In addition, we compared the parameters of VT among subjects with and without cigarette smoking and exercise habits [A: cigarette smoking (+) exercise habits (+), B: cigarette smoking (−) exercise habits (+), C: cigarette smoking (+) exercise habits (−), D: cigarette smoking (−) exercise habits (−)] (Table 4). In men, oxygen uptake at VT in group C and D was significantly lower than that in group A and B. Work rate at VT in group C and D was significantly lower than that in group B. No significant differences of heart rate were not noted among the four groups. In women, oxygen uptake at VT in group C was significantly lower than that in group A and B. Work rate at VT in group A was significantly higher than that in group B, C, and D. Heart rate at VT in group D was significantly higher than that in group B. Oxygen uptake at VT in group A and B (with exercise habits) was higher than that in group C and D (without exercise habits) in both sexes, as in our previous report [5].

Finally, we evaluated the relationship between the number of cigarettes smoked per day and oxygen uptake at VT, and also between the BI and oxygen uptake at VT (Fig. 1). The number of cigarettes smoked per day was not correlated with oxygen uptake at VT in either sex (men $r = -0.172$, $p = 0.0265$; women $r = -0.294$, $p = 0.0470$). BI was also not clearly correlated with oxygen uptake at VT (men $r = -0.192$, $p = 0.0132$; women $r = -0.214$, $p = 0.1535$). In subjects without exercise habits, the number of cigarettes smoked per day was not correlated with oxygen uptake at VT in either sex (men $r = -0.072, p = 0.4487$; women $r = -0.180, p = 0.2791$). BI was also not clearly correlated with oxygen uptake at VT (men $r = -0.135$, $p = 0.1515$; women $r = -0.088$, $p = 0.5976$).

Discussion

Impairment of pulmonary oxygen exchange [13, 14], downregulation of adrenergic receptors [15], and long-term cardiac damage caused by stimulation of catecholamine by smoking [16] may also in part explain lower oxygen uptake at VT in subjects with cigarette smoking. Some cross-sectional studies show that cigarette smoking is correlated with cardiovascular fitness [17–19]. Hirsch et al. [17] evaluated the immediate effects of cigarette smoking on aerobic exercise capacity, and cigarette smoking resulted in a significantly lower $\dot{V}O_{2\,max}$ and higher heart rate after 3 cigarettes/h for 5 h. Marti et al. [18] reported that, among army conscripts, the distance covered in a 12-min endurance run was inversely related to daily cigarette consumption and years of smoking. Rotstein et al. [19] also reported that smoking retards physiological responses to submaximal exercise immediately after smoking three cigarettes. In a longitudinal analysis, Sandvik et al. [20] showed that decline in physical fitness and lung function was greater among smokers than that among nonsmokers

Table 4 Comparison of parameters at ventilatory threshold among subjects with and without cigarette smoking and exercise habits

	A Cigarette smoking (+) Exercise habits (+)	B Cigarette smoking (−) Exercise habits (+)	C Cigarette smoking (+) Exercise habits (−)	D Cigarette smoking (−) Exercise habits (−)
Men				
Number of subjects	52	112	114	129
Oxygen uptake at ventilatory threshold (ml/kg/min)	15.6 ± 3.7	16.9 ± 5.4	13.8 ± 2.6^{ab}	13.8 ± 2.5^{ab}
Work rate at ventilatory threshold (W)	84.8 ± 25.2	92.5 ± 31.8	77.5 ± 18.0^{b}	78.6 ± 18.8^{b}
Heart rate at ventilatory threshold (beats/min)	103.8 ± 12.2	104.7 ± 13.3	106.2 ± 10.3	107.7 ± 11.6
Women				
Number of subjects	8	97	38	275
Oxygen uptake at ventilatory threshold (ml/kg/min)	14.4 ± 5.0	13.2 ± 3.3	11.5 ± 1.8^{ab}	12.4 ± 2.1
Work rate at ventilatory threshold (W)	70.0 ± 27.0	53.2 ± 17.3^{a}	49.3±13.5^{a}	50.3 ± 12.8^{a}
Heart rate at ventilatory threshold (beats/min)	105.6 ± 13.3	104.1 ± 12.0	106.3±11.2	108.2 ± 11.7^{b}

Mean ± SD

[a] $p < 0.05$ versus cigarette smoking (+), exercise habits (+)

[b] $p < 0.05$ versus cigarette smoking (−), exercise habits (+)

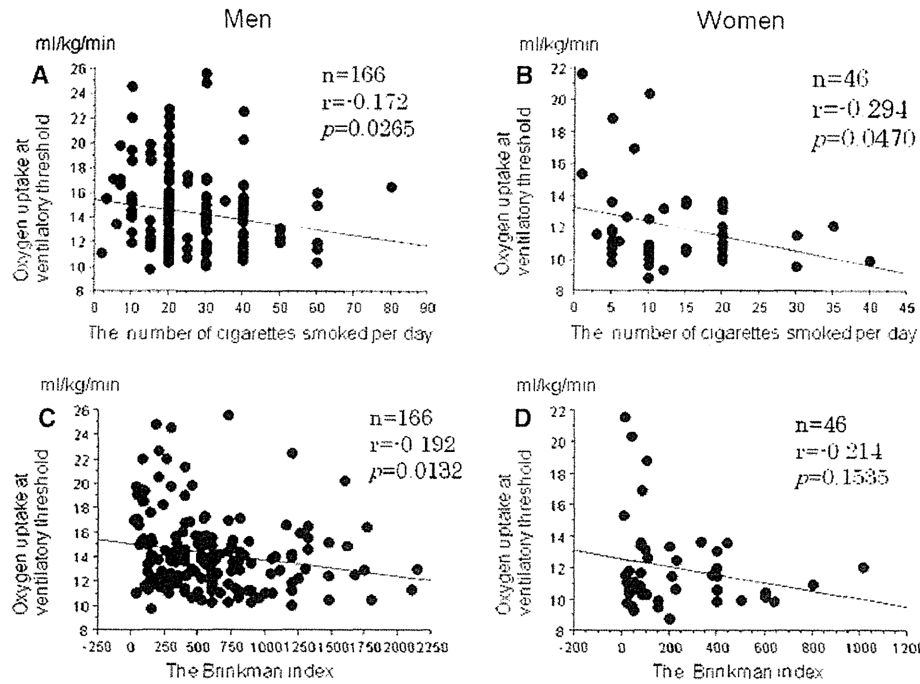

Fig. 1 Simple correlation analysis between the number of cigarettes smoked per day and oxygen uptake at ventilatory threshold (**a** men, **b** women), and between the Brinkman Index and oxygen uptake at ventilatory threshold (**c** men, **d** women)

among 1,393 men over 7 years. In this study, we solely evaluated the relationship between cigarette smoking and aerobic exercise level defined by VT in the Japanese. Exercise habits were closely linked to cigarette smoking in men, and the differences of parameters at VT between subjects with and without cigarette smoking were attenuated after adjusting for age and exercise habits. However, in women without exercise habits, oxygen uptake at VT in women with cigarette smoking was significantly lower than that in women without, after adjusting for age. In addition, we compared oxygen uptake at VT among subjects with and without cigarette smoking and exercise habits, and found that oxygen uptake at VT in group B was highest among four groups in men. Oxygen uptake at VT in group C was lowest among four groups in both sexes. Taken together, a combination of promoting exercise habits and prohibiting cigarette smoking might be considered for improving aerobic exercise level, especially in women.

Potential limitations still remain in this study. First, our study was a cross-sectional and not a longitudinal study. Second, 407 men and 418 women in our study voluntarily underwent measurements; they were therefore more likely to be health conscious compared with the average person. Third, we could not show a clear relation between cigarette smoking and oxygen uptake at VT. Fourth, the relationship between cigarette smoking and exercise habits was not noted in women. The low prevalence of subjects with exercise habits and cigarette smoking might affect the results. However, it seems reasonable to suggest that prohibiting smoking and promoting exercise habits might result in amelioration of aerobic exercise level in some Japanese. Sandvik et al. [21] reported that physical fitness was a graded, independent, long-term predictor of mortality from cardiovascular causes in healthy, middle-aged men. To show this, further prospective studies are needed in the Japanese.

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