きる可能性を示唆している．男性を対象にしたいくつかの研究では，心肺体力が高いからといって必ずしも血糖や血圧が低いわけではないことが報告されている8,22,26)．これらの値には，いずれも身体活動などの生活習慣に加え，食生活や遺伝的素因が関連する諸因子が大きく影響することが知られている．

以上述べてきたように，心肺体力の低い男性では，腹囲，血中脂質および血圧の項目が，心肺体力の低い女性では腹囲，血中脂質，血圧に加え血糖の項目が，高いMSリスクに関与していたと考えられ，その結果，男女とも心肺体力が高い群では低い群に比べてMSリスクが低かったと考えられる．そこで，MSリスクが異なる集団において心肺体力に差があるか否かを検証することとした．被験者を低リスク群（リスク保有数0または1）と高リスク群（リスク保有数2以上）に分類し，年齢に対する$\dot{V}O_2max$の差を検討したところ，男性では両群の回帰直線の傾きには有意な差が認められなかった（Fig. 2A）．したがって，MSリスクの異なる男性において，加齢による$\dot{V}O_2max$低下は同程度であったと考えられる．また，男性においては低リスク群は高リスク群よりy切片が有意に高い値を示したため，MSリスクの低い男性は，高い男性に比べて$\dot{V}O_2max$が有意に高いことが示唆される．一方，女性では，MSリスクの高い群においては，年齢と$\dot{V}O_2max$の間に相関関係がみられなかった（Fig. 2B）．閉経後女性では，若年女性に比べて体脂肪率が高い一方で除脂肪量が少なく，心肺体力も低いと報告されている27)．また，内臓脂肪蓄積が閉経後の期間によく相関することが指摘されている28)．本研究においても，女性では，これらの指標についての閉経というライフイベントによる身体的変化が，年齢より強くMSリスクに影響しているのかもしれない．

最後に，MSリスクの低い群の$\dot{V}O_2max$と“EPAR 2006”で基準とされた心肺体力との関係を検討するために，“健康づくりのための最大酸素摂取量”の「基準値」および「範囲」の下限値をFig. 2AおよびFig. 2Bに示した．男女ともMSリスクの低い群の$\dot{V}O_2max$の加齢変化を示す回帰直線は，「基準値」とほぼ一致していたことより，MSリスクの低い人は，“健康づくりのための最大酸素摂取量”の「基準値」程度の心肺体力を保持していることが示唆される．

$\dot{V}O_2max$は，身体活動量を比較的よく反映すると報告されている29)．また，$\dot{V}O_2max$を向上させるためには，一定の強度以上で身体活動を行うことが重要であるとの指摘もある30)．Simmonsら31)は，コホート研究によって身体活動量および心肺体力の変化とMSリスクとの関係を明らかにしており，我が国においても今後，$\dot{V}O_2max$などの体力指標だけでなく，日常生活の身体活動量やその強度がMSリスクに及ぼす影響を調査・検討し，MS予防のための身体活動の量さらにはその強度を示す必要があるだろう．

Ⅵ．まとめ

日本人中高年者を対象とした本研究では，男性では心肺体力が“健康づくりのための最大酸素摂取量”の「基準値」より低いとMSリスクが高く，女性では「範囲」を下回っているとMSリスクが高いことが示された．特に，心肺体力の低い男性において，MSリスクが高いことが示唆された．心肺体力が高い中高年者では，MSを発現しにくいことが示唆される．これらの結果は，心肺体力が“健康づくりのための最大酸素摂取量”の「基準値」および「範囲」より低い場合，$\dot{V}O_2max$を高めるような身体活動を推奨する根拠の一部を提示しているといえるだろう．

謝　辞
本研究は，平成19～20年度厚生労働科学研究費補助金（循環器疾患等生活習慣病対策総合研究事業　健康づくりのための運動基準・エクササイズガイド改定に関する研究　主任研究者　田畑泉）によって行われた．本研究にご協力いただいた被験者の皆様に心より感謝いたします．

（受理日　平成21年4月4日）

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European Journal of Clinical Nutrition (2009) 63, 465–472

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ORIGINAL ARTICLE

Muscle mass and bone mineral indices: does the normalized bone mineral content differ with age?

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Objective: To investigate the relationships between regional skeletal muscle mass (SM mass) and bone mineral indices and to examine whether bone mineral content (BMC) normalized to SM mass shows a similar decrease with age in young through old age.

Subjects/Methods: One hundred and thirty-eight young and postmenopausal women aged 20–76 years participated in this study and were divided into three groups: 61 young women, 49 middle-aged postmenopausal women and 28 older postmenopausal women. Muscle thickness (MTH) was determined by ultrasound, and regional SM mass (arm, trunk and leg) was estimated based on nine sites of MTH. Whole-body and regional lean soft tissue mass (LSTM), bone mineral density (BMD) and BMC (whole body, arms, legs and lumbar spine) were measured using dual-energy X-ray absorptiometry.

Results: Ultrasound spectroscopy indicated that SM mass is significantly correlated with site-matched regional bone mineral indices and these relationships correspond to LSTM. The BMC and BMD in older women were significantly lower than those in middle-aged women. When BMC was normalized to site-matched regional SM mass, BMC normalized to SM mass in arm and trunk region were significantly different with age; however, whole-body and leg BMC normalized to SM mass showed no significant difference between middle-aged and older postmenopausal women.

Conclusions: The age-related differences in BMC were found to be independent of the ageing of SM mass in the arm and trunk region. However, differences in BMC measures of the leg and whole body were found to correspond to age-related decline of SM mass in postmenopausal women.

European Journal of Clinical Nutrition (2009) **63,** 465–472; doi:10.1038/sj.ejcn.1602977; published online 23 January 2008

Keywords: age; bone mineral content; bone mineral density; muscle function; skeletal muscle mass; ultrasound

Introduction

Fractures in the elderly are associated with the loss of bone mineral density (BMD) and an increased risk of falls (Pfeifer *et al.*, 2004). Femoral neck and lumbar fractures are especially common problems in the elderly and can have a devastating impact on their ability to remain independent. Many investigators have shown that muscle strength (Gleeson *et al.*, 1990; Peterson *et al.*, 1991; Blain *et al.*, 2001; Sinaki *et al.*, 2002) and muscle mass (Pluijm *et al.*, 2001; Szulc *et al.*, 2005; Walsh *et al.*, 2006) are associated with site-matched bone mineral indices, that is, BMD or bone mineral content (BMC). The greater rates of age-related loss of skeletal muscle mass (SM mass) occur in the legs and lower trunk regions, while only moderate losses occur in the upper trunk and arm regions (Reimers *et al.*, 1998; Kanehisa *et al.*, 2004). These regions correspond to the segments where fractures occur frequently. However, it is not sufficiently clear whether the age-related decrease of regional SM mass (for example, arm, leg and trunk region) affects the age-related decline of bone mineral indices in postmenopausal women.

According to Schiessl *et al.* (1998), more bone mass is accrued per lean body mass after puberty in girls than in boys. It has been speculated that this bone mass is not mechanically needed and serves as a surplus for

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Received 11 July 2007; revised 31 October 2007; accepted 22 November 2007; published online 23 January 2008

reproduction. Schonau (2004) has repeated this finding in more depth in a series of papers based upon the forearm, but other authors (Ferretti *et al.*, 2000; Rittweger *et al.*, 2000) were unable to detect the surplus bone in the lower body. The accelerated bone loss observed around menopause is predominantly due to oestrogen deficiency (Kassem *et al.*, 1996). The phase of rapid bone loss normally lasts 4–8 years, and after this period, age-related bone loss is considered to occur in women.

Although the dual-energy X-ray absorptiometry (DXA) method can be used to accurately estimate SM mass (appendicular muscle mass), it is not capable of accurate distinguish of SM mass from the trunk region. Ultrasound muscle thickness (MTH) has been widely employed for accurate measurement of SM size *in vivo* (Kawakami *et al.*, 1993; Abe *et al.*, 1997; Reimers *et al.*, 1998), and previous studies have shown it to be highly reliable and valid in measuring MTH (Kawakami *et al.*, 1993; Reimers *et al.*, 1998). These characteristics make ultrasound a useful alternative to other more expensive imaging methods for assessing changes in SM mass. Moreover, ultrasound-derived prediction equations can accurately estimate the regional SM mass involving the measurement of arm, leg and trunk muscles (Sanada *et al.*, 2006).

The present cross-sectional study investigates the relationships between regional SM mass and bone mineral indices, and examines whether regional BMC normalized to SM mass shows a similar decrease with age in young subjects through old age.

Methods

Subjects

One hundred and thirty-eight young and postmenopausal women aged 20–76 years participated in this study and were divided into three groups: 61 young women (YW: 23.7 ± 0.5, 20–39 years), 49 middle-aged postmenopausal women (MW: 58.3 ± 0.6, 40–64 years) and 28 older postmenopausal women (OW: 70.3 ± 0.7, 65–76 years). The NASA/JSC physical activity scale, a questionnaire method, was used to survey the subject's physical activity (Ross and Jacson, 1990). This scale was developed to provide an assessment score of 0–7 on a person's level of regular physical activity. There are a series of eight statements about routine physical activity.

None of the subjects smoked and they were not taking any medications, such as β-blockers, steroids or hormone replacement therapy. The subjects involved in this study were both sedentary and active women. Active young women participated in continuous aerobic exercise for at least one session per week for 1 h per session. Active postmenopausal women participated in a swimming programme for at least two sessions per week for 1 h per session. However, they were not highly trained athletes.

The purpose, procedures and risks of the study were explained to each participant prior to inclusion, and all subjects gave their written informed consent before participating in the study approved by the Human Research Committee of the National Institute of Health and Nutrition. The study was performed in accordance with the guidelines of the Declaration of Helsinki.

Whole-body DXA

Lean soft tissue mass (LSTM), fat mass, BMC and BMD were determined for the whole body using DXA (Hologic QDR-4500A scanner; Hologic, Waltham, MA, USA). Subjects were positioned for whole-body scans according to the manufacturer's protocol. Participants lay in the supine position on the DXA table with the limbs close to their bodies. The bone densitometer delivers a very low dose of radiation (1.5 mR for the whole body) using quantitative digital radiography. Daily DXA calibration of phantoms showed a coefficient of variation of 0.35% for BMD over the past 156 measurement points. The whole-body BMC and LSTM were divided into several regions, that is, arms, legs, trunk and head. The body compositions were analysed using manual DXA analysis software (version 11.2:3). The arm region was defined as the region extending from the head of the humerus to the distal tip of the fingers. The reference point between the head of the humerus and the scapula was positioned at the glenoid fossa. The leg region was defined as the region extending from the inferior border of the ischial tuberosity to the distal tip of the toes. The whole body was defined as the region extending from the shoulders to the distal tip of the toes. To minimize inter-observer variation, all scans and analyses were carried out by the same investigator, and the day-to-day coefficient of variations of his observations were 0.72% for BMD, 2.95% for LSTM and 6.98% for fat mass in the whole body.

Blood samples

Before all measurements, fasting (>12 h) blood samples were collected by venipuncture in EDTA-containing tubes, refrigerated immediately and centrifuged at 1500 r.p.m. for 30 min at 4 °C within 2 h. Serum samples from each participant were stored frozen at −20 °C. Estradiol was assessed by radioimmunoassay (Amersham Biosciences, Piscataway, NJ, USA). In postmenopausal women, menopausal status was confirmed by concentrations of estradiol less than 20 pg ml^{-1}. In this study, estradiol concentrations were 11.4 ± 0.3 pg ml^{-1} (range of 10.0–17.0 pg ml^{-1}) in MW and 11.8 ± 0.4 pg ml^{-1} (range of 10.0–16.0 pg ml^{-1}; Table 1) in OW. Serum intact osteocalcin was measured with a sandwich enzyme immunoassay that uses polyclonal antibodies against 20 N-terminal residues (amino acids 1–20) and against seven C-terminal residues (amino acids 43–49; MBC, Tokyo, Japan). The inter- and intra-assay coefficient of variations for the estradiol and osteocalcin were <10%.

Ultrasound MTH and measurements

Muscle thickness determined by B-mode ultrasound was assessed at nine sites on the anterior and posterior surfaces of

Table 1 Physical characteristics of subjects

	Young (n = *61*)	*Middle* (n = *49*)	*Old* (n = *28*)
Age (years)	23.7 ± 0.5	58.3 ± 0.6^{a}	70.3 ± 0.7^{a,b}
Age at menopause (years)		50.0 ± 0.6	50.1 ± 0.9
Years since menopause		8.3 ± 0.7	20.2 ± 1.1^{b}
Serum estradiol (pg ml^{-1})	86.4 ± 8.2	11.4 ± 0.3^{a}	11.8 ± 0.4^{a}
Osteocalcin (pg ml^{-1})	5.47 ± 0.3	9.7 ± 0.4^{a}	9.9 ± 0.6^{a}
Body mass (kg)	51.8 ± 0.7	55.4 ± 1.0^{a}	52.6 ± 1.0^{b}
BMI (kg m^{-2})	20.2 ± 0.2	23.3 ± 0.4^{a}	22.6 ± 0.5^{a}
Percent body fat (%)	24.6 ± 0.6	31.2 ± 0.9^{a}	30.3 ± 0.7^{a}
VO_2peak (ml kg^{-1} min^{-1})	33.8 ± 0.7	29.3 ± 0.7^{a}	24.6 ± 0.8^{a,b}
Handgrip strength (kg)	28.9 ± 0.7	27.2 ± 0.6	23.4 ± 0.7^{a,b}
Leg extension power (W kg^{-1})	17.3 ± 0.6	13.8 ± 0.5^{a}	12.5 ± 0.7^{a}
Physical activity scale	4.2 ± 0.2	4.7 ± 0.2	4.2 ± 0.3

Abbreviations: BMI, body mass index; VO_2peak, peak oxygen uptake.
Data are presented as means ± s.e.m.
[a] Significantly different from young, $P<0.05$.
[b] Significantly different from middle-aged, $P<0.05$.

the body as described previously by Abe *et al.* (1994). The sites were lateral forearm, anterior and posterior upper arm, abdomen, subscapula, anterior and posterior thigh, and anterior and posterior lower leg. Ultrasonographic evaluation of MTH was performed using a real-time linear electronic scanner with a 5 MHz scanning head (SSD-500; Aloka, Tokyo, Japan). The scanning head with water-soluble transmission gel was placed perpendicular to the tissue interface at the marked sites and provided acoustic contact without depression of the skin surface. MTHs were measured directly from the screen with electronic callipers, and determined as a distance from the adipose tissue–muscle interface to the muscle–bone interface. Whole-body and regional SM mass were estimated using the equations of Sanada *et al.* (2006). MTHs were converted to mass units in kilograms by ultrasound-derived prediction equations using site-matched MTH × height, which were then used to calculate arm, trunk, thigh and lower leg SM mass. The reliability of image reconstruction and distance measurements were confirmed by comparing the ultrasonic and manual measurements of tissue thickness in human cadavers, and the coefficient of variation for the MTH measurements was 1% (Kawakami *et al.*, 1993).

Measurement of fitness values

The peak oxygen uptake (VO_2peak) was measured by an incremental cycle exercise test using a cycle ergometer (Monark, Varberg, Sweden). The subjects were encouraged during the ergometer test to exercise at the level of maximum intensity. Subjects breathed through a low-resistance two-way valve, and the expired air was collected in Douglas bags. Expired O_2 and CO_2 gas concentrations were measured by mass spectrometry (WSMR-1400; Westron, Chiba, Japan), and gas volume was determined using a dry gas metre (NDS-2A-T; Shinagawa Dev., Tokyo, Japan). The system of mass spectrometer was calibrated during every measurement by the standard reference gas. The highest value of VO_2 during the exercise test was designated as VO_2peak.

Leg extension power was measured with an isokinetic leg power system (Anaero Press 3500; Combi wellness, Tokyo, Japan) in the sitting position. Handgrip strength of the right upper limb was measured with a hand-held dynamometer, with the subject standing and arms extended by their side.

Statistical analysis

All measurements and calculated values are expressed as the mean ± s.e.m. We compared the mean values of general criteria, bone mineral indices, body composition values and fitness values among the three age groups using one-way analysis of variance with body mass index (BMI) adjusted for the covariate. In cases with a significant F-value, a *post-hoc* test using the Newman–Keuls method was used to identify significant differences among the mean values. Pearson's product correlations were calculated between LSTM, SM mass or fitness values and bone mineral indices. The α level for testing significance was set at $P<0.05$. All statistical analyses were performed using Stat View v5.0 for Windows (SYS Institute).

Results

The physical characteristics of the subjects are presented in Table 1. The BMI and body fat percentage in MW and OW were significantly higher than those in YW ($P<0.05$). There were no significant differences in the NASA/JSC physical activity scale among the groups. Serum estradiol in MW and OW were significantly lower than those in YW ($P<0.05$). Serum osteocalcin in MW and OW were significantly higher than those in YW ($P<0.05$). Handgrip strength in OW was significantly lower than that in YW and MW ($P<0.05$). Leg extension power in MW and OW were significantly lower than those in YW ($P<0.05$). VO_2peak (normalized to body mass) in MW and OW were significantly lower than those in YW ($P<0.05$).

Age-related decline of body composition and bone mineral indices

Leg SM mass and LSTM in MW and OW were significantly lower than those in YW ($P<0.05$, Table 2). Leg SM mass in OW was significantly lower than that in MW ($P<0.05$), but there was no such difference in leg LSTM. Table 3 shows the mean BMC, BMD and bone mineral indices normalized to SM mass. The BMC and BMD in MW and OW were significantly lower than those in YW ($P<0.05$), while BMC (whole body, arms, trunk and legs) and BMD (whole body, arms and legs) in OW were significantly lower than in those MW ($P<0.05$). The BMC normalized to SM mass in MW and OW was significantly lower than that in YW ($P<0.05$). The arm BMC normalized to arm SM mass and the trunk BMC normalized to trunk SM mass in OW were significantly lower than those in MW. However, whole-body and leg BMC normalized to leg SM mass were not significantly different between MW and OW. Furthermore, the interaction (age × BMI) of the age-related differences of BMD, BMC and normalized BMC was not significant.

There was significantly negative correlation between age and BMC normalized to SM mass in all women ($P<0.001$, Table 4). However, when the subjects were divided into three age groups, there was no significant correlation between age and BMC normalized to SM mass in middle-aged and older women.

Table 2 Skeletal muscle mass estimated by ultrasound and LSTM and fat mass measured by DXA

Variables	*Body segments*	*Young (n = 61)*	*Middle (n = 49)*	*Old (n = 28)*
SM mass (kg)	Whole body	14.3 ± 0.3	13.7 ± 0.3	12.0 ± 0.4^{a,b}
	Arm	1.4 ± 0.0	1.4 ± 0.0	1.3 ± 0.0^{a,b}
	Trunk	6.0 ± 0.0	5.8 ± 0.1	5.5 ± 0.1^{a,b}
	Leg	7.3 ± 0.1	6.9 ± 0.1^{a}	6.1 ± 0.2^{a,b}
LSTM (kg)	Whole body	34.3 ± 0.5	34.1 ± 0.5	32.4 ± 0.6^{a,b}
	Arm	3.2 ± 0.1	3.2 ± 0.1	3.1 ± 0.1
	Trunk	18.4 ± 0.2	18.8 ± 0.3	17.8 ± 0.3^{b}
	Leg	12.8 ± 0.2	12.1 ± 0.2^{a}	11.6 ± 0.3^{a}
Fat mass (kg)	Whole body	12.8 ± 0.4	17.4 ± 0.7^{a}	16.0 ± 0.6^{a,b}
	Arm	1.5 ± 0.1	2.0 ± 0.1^{a}	1.8 ± 0.1^{a}
	Trunk	4.8 ± 0.2	9.0 ± 0.4^{a}	8.1 ± 0.4^{a,b}
	Leg	6.2 ± 0.2	6.3 ± 0.2	5.8 ± 0.2

Abbreviations: DXA, dual-energy X-ray absorptiometry; LSTM, lean soft tissue mass; SM mass, skeletal muscle mass.
Data are presented as means ± s.e.m.
[a]Significantly different from young, $P<0.05$.
[b]Significantly different from middle-aged, $P<0.05$.

Relationships between SM mass, muscle functions and bone mineral indices

Lean soft tissue mass was significantly correlated with site-matched BMC (arm, trunk, leg and whole body; $r=0.57$, 0.73, 0.53 and 0.47, respectively; $P<0.05$, Figure 1) and BMD (arm, L-spine, leg and whole body; $r=0.38$, 0.40, 0.60 and 0.42, respectively; $P<0.05$, Figure 2). These associations corresponded to the relationships between SM mass measured by ultrasound and the site-matched BMC (arm, trunk, leg and whole body; $r=0.53$, 0.49, 0.66 and 0.55, respectively; $P<0.05$, Figure 1) and BMD (arm, L-spine, leg and whole body; $r=0.38$, 0.44, 0.55 and 0.52, respectively; $P<0.05$, Figure 2) in all women. The BMD in YW, MW and OW is also significantly correlated with the site-matched SM mass; $r=0.29$–0.54, 0.36–0.44 and 0.46–0.60, respectively ($P<0.05$). The correlation coefficients in OW were comparatively higher than those in YW or MW. In older women, absolute $\dot{V}O_2$peak ($\mathrm{l\,min^{-1}}$) was not significantly correlated with whole-body BMD (Table 5). Moreover, the absolute leg extension power (W) and leg extension power normalized to body mass ($\mathrm{W\,kg^{-1}}$) were significantly correlated with leg BMD, but not leg extension power normalized to leg SM mass ($\mathrm{W\,kg^{-1}}$).

Discussion

This study investigated the relationships between regional SM mass and bone mineral indices, and sought to determine whether regional BMC normalized to SM mass showed a similar decrease with age in young subjects through old age.

Table 3 Age-related differences of bone mineral density, bone mineral and bone mineral content normalized to SM mass

Variables	*Body segments*	*Young (n = 61)*	*Middle (n = 49)*	*Old (n = 28)*
BMD (g cm ^{2})	Whole body	1.12 ± 0.01	0.99 ± 0.01^{a} (12%)	0.91 ± 0.01^{a,b} (8%)
	Arm	0.71 ± 0.01	0.63 ± 0.01^{a} (11%)	0.59 ± 0.01^{a,b} (6%)
	L-spine	1.07 ± 0.02	0.92 ± 0.02^{a} (14%)	0.86 ± 0.03^{a} (7%)
	Leg	1.12 ± 0.01	1.01 ± 0.01^{a} (10%)	0.94 ± 0.02^{a,b} (7%)
BMC (g)	Whole body	1796 ± 47	1350 ± 42^{a} (25%)	1175 ± 39^{a,b} (13%)
	Arm	238 ± 4	199 ± 5^{a} (16%)	174 ± 5^{a,b} (13%)
	Trunk	551 ± 12	451 ± 12^{a} (18%)	388 ± 11^{a,b} (14%)
	Leg	741 ± 14	600 ± 15^{a} (19%)	544 ± 16^{a,b} (9%)
BMC normalized to SM mass (g kg ^{1})	Whole body	127 ± 3	99 ± 2^{a} (22%)	100 ± 4^{a} (−1%)
	Arm	175 ± 2	144 ± 3^{a} (18%)	134 ± 3^{a,b} (7%)
	Trunk	93 ± 2	78 ± 2^{a} (16%)	71 ± 2^{a,b} (9%)
	Leg	102 ± 2	87 ± 2^{a} (15%)	91 ± 2^{a} (−5%)

Abbreviations: BMC, bone mineral content; BMD, bone mineral density; SM mass, skeletal muscle mass.
The percentage of differences were calculated from the value from young versus middle-aged and middle-aged versus old. Data are presented as means ± s.e.m.
[a]Significantly different from young, $P<0.05$.
[b]Significantly different from middle-aged, $P<0.05$.

Table 4 Correlation coefficients between age and measurement variables in young and postmenopausal women

Variables	*Body segments*	*Total (n = 138)*	*Young (n = 61)*	*Middle (n = 49)*	*Old (n = 28)*
BMD (g cm ^{2})	Whole body	−0.73***	0.00	−0.30*	−0.52***
	Arm	−0.75***	0.13	−0.24	−0.56***
	L-spine	−0.53***	0.04	−0.28	−0.40***
	Leg	−0.64***	0.01	−0.11	−0.39***
BMC (g)	Whole body	−0.67***	−0.40***	−0.16	−0.32
	Arm	−0.66***	0.13	−0.26	−0.54***
	Trunk	−0.64***	−0.05	−0.26	−0.24
	Leg	−0.63***	0.11	−0.13	−0.42***
LSTM (kg)	Whole body	−0.16	−0.02	−0.02	−0.25
	Arm	−0.07	−0.05	0.02	−0.27
	Trunk	−0.04	0.02	−0.09	−0.27
	Leg	−0.29**	−0.03	0.06	−0.17
SM mass (kg)	Whole body	−0.35***	0.03	−0.08	−0.44***
	Arm	−0.09	0.16	−0.13	−0.55***
	Trunk	−0.32***	−0.24	−0.20	−0.35
	Leg	−0.34***	−0.02	0.00	−0.23
BMC normalized to SM mass (g kg ^{1})	Whole body	−0.55***	−0.45***	−0.12	0.08
	Arm	−0.70***	−0.01	−0.20	−0.09
	Trunk	−0.55***	0.13	−0.14	0.02
	Leg	−0.41***	0.07	−0.12	−0.15

Abbreviations: BMC, bone mineral content; BMD, bone mineral density; LSTM, lean soft tissue mass; SM mass, skeletal muscle mass.
*$P<0.05$; **$P<0.01$; ***$P<0.001$.

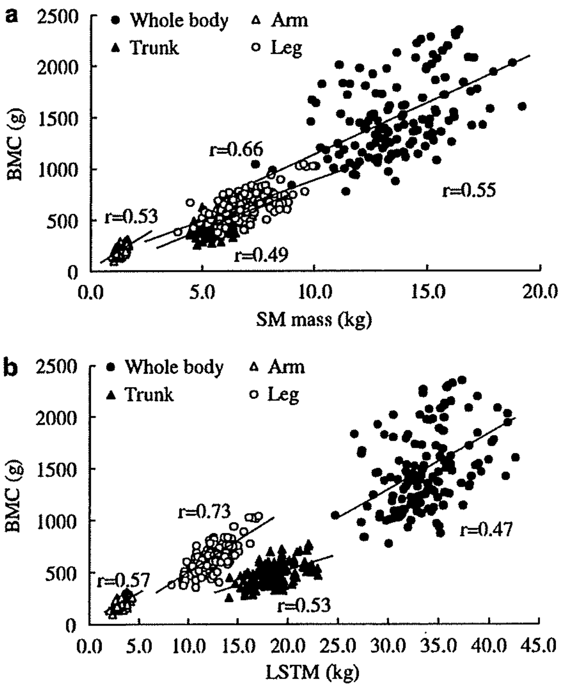

Figure 1 Relationship between SM mass estimated by ultrasound (a) or LSTM (b) measured by DXA and BMC in all subjects ($n = 138$). Whole-body and regional SM mass and LSTM were significantly correlated with BMC in all body segments ($P<0.05$). BMC, bone mineral content; DXA, dual-energy X-ray absorptiometry; LSTM, lean soft tissue mass; SM mass, skeletal muscle mass.

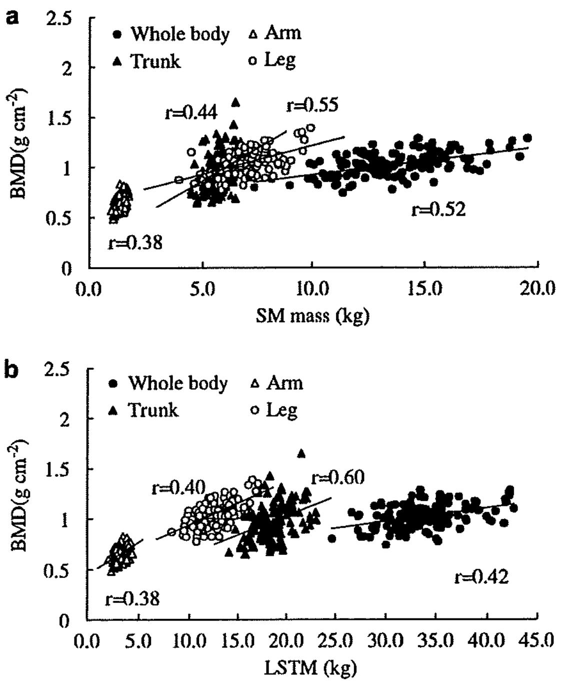

Figure 2 Relationship between SM mass estimated by ultrasound (a) or LSTM (b) measured by DXA and BMD in all subjects ($n = 138$). Whole-body and regional SM mass and LSTM were significantly correlated with BMD in all body segments ($P<0.05$). BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; LSTM, lean soft tissue mass; SM mass, skeletal muscle mass.

Table 5 Correlation coefficients between fitness value and BMD in young and postmenopausal women

	VO_2peak versus whole-body BMD			*Handgrip strength versus arm BMD*			*Leg extension power versus leg BMD*		
	Absolute ($l\,min^{-1}$)	*Normalized to body mass ($ml\,kg^{-1}\,min^{-1}$)*	*Normalized to total SM mass ($ml\,kg^{-1}\,min^{-1}$)*	*Absolute (kg)*	*Normalized to body mass ($kg\,kg^{-1}$)*	*Normalized to arm SM mass ($kg\,kg^{-1}$)*	*Absolute (W)*	*Normalized to body mass ($W\,kg^{-1}$)*	*Normalized to leg SM mass ($W\,kg^{-1}$)*
Young (*n*=61)	0.43***	0.30*	0.08	0.47***	0.37**	0.20	0.61***	0.49***	0.41***
Middle (*n*=49)	0.47***	0.17	0.09	0.34*	0.14	0.05	0.26	0.06	0.09
Old (*n*=28)	0.32	0.02	−0.18	0.42*	0.15	0.01	0.60***	0.46*	0.37

Abbreviations: BMD, bone mineral density; SM mass, skeletal muscle mass.
*$P<0.05$; **$P<0.01$; ***$P<0.001$.

The major findings of this cross-sectional study were as follows: (1) SM mass were associated with the site-matched bone mineral indices, and these associations corresponded to the relationships between LSTM and the site-matched bone mineral indices; (2) BMC normalized to SM mass estimated by ultrasound in arm and trunk region were also significantly different with age, but not in leg and whole body in middle-aged and older postmenopausal women. These results suggest that the age-related decline of BMC normalized to SM mass was different in the body segments. Thus, the age-related differences in BMC were found to be independent of the ageing of SM mass in the arm and trunk region. However, differences in BMC measures of the leg and whole body were found to correspond to age-related decline of SM mass in postmenopausal women.

Age-related decline in SM mass and bone mineral indices

As both SM mass and bone mineral indices decrease with age, it is not yet clear how the age-related decrease in SM mass (for example, arm, leg and trunk region) affects the age-related decline of bone mineral indices in young and postmenopausal women. The age-related differences in BMC normalized to the site-matched SM mass in MW were significantly lower than those in YW (15–22%, Table 3), and serum estradiol in MW were also significantly lower than those in YW (87%, $P<0.05$, Table 1). In addition, serum estradiol in MW was significantly lower than that in YW. These results suggest that age-related decrease of BMC from youth through middle age was associated with age-related change of oestrogen deficiency (NIH Consensus Development Panel on Osteoporosis Prevention, 2001). However, when postmenopausal women were divided into MW and OW, age-related differences in whole-body and leg BMC normalized to SM mass were absent in older postmenopausal women (Table 3) with no changes in serum estradiol and osteocalcin. Furthermore, the interaction (age × BMI) of the age-related differences of BMD, BMC and normalized BMC was not significant. Therefore, the age-related differences in whole-body and leg BMC among middle-aged and older postmenopausal women were considered partly due to the age-related changes in SM mass independent of the differences of BMI. These results support that the preservation of ageing of muscles is an important factor for maintenance of leg and whole-body BMC, especially in older women.

Relationships between SM mass, muscle function and bone mineral indices

The SM mass were associated with the site-matched bone mineral indices, and these associations show equivalent to better correlations among LSTM determined by DXA and the site-matched bone mineral indices. The final outcome is so much stronger when adjusted data use independent measurements. Every DXA-derived component from BMC to FM to LSTM is likely to co-vary, since they are all derived from the same scan. These results can be applied to the future studies such as the development of prediction equation for bone mineral indices using ultrasound technique. A compact-type ultrasound machine weighs approximately 3 kg, making it easily portable. Ultrasound-derived prediction equations are capable of taking measurements in the field, and are safe and valid in predicting total and regional SM mass (Sanada *et al*., 2006).

Some investigators have shown that prolonged low-to-moderate intensity exercise is independently associated with higher BMD (Nguyen *et al*., 1998; Hagberg *et al*., 2001; Pongchaiyakul *et al*., 2004), while cardiorespiratory fitness (VO_2peak) is only slightly correlated with bone mineral indices (Henderson *et al*., 1995; Ryan and Elahi, 1998; Ryan *et al*., 1998; Lynch *et al*., 2002). In this study, VO_2peak (normalized to body mass) in young women was significantly correlated with BMD ($P<0.05$), while VO_2peak (normalized to whole-body SM mass) was not significantly associated with BMD (Table 5). These results indicate that although the present and previous studies have shown aerobic fitness to be associated with BMD, this relationship may be due to the magnitude of SM mass. However, in older women, even absolute VO_2peak ($l\,min^{-1}$) was not significantly correlated with whole-body BMD. In the same way, low grip strength is associated with low BMD and an increased risk of incident vertebral fracture (Bevier *et al*., 1989; Osei-Hyiaman *et al*., 1999; Di Monaco *et al*., 2000; Dixon *et al*., 2005). The absolute handgrip strength in older women were significantly correlated with BMD, but not normalized to body mass and SM mass, in present study. These results suggest the relation of BMD and handgrip strength associated with body mass. However, the absolute leg extension power (W) and leg extension power normalized to body mass ($W\,kg^{-1}$) were significantly correlated with leg BMD, but not normalized to leg SM mass ($W\,kg^{-1}$). There is no difference in leg BMC (normalized to SM) between middle-aged and older women, there may be a difference but this study does not have the power to demonstrate a difference, particularly as the numbers are much less in the older groups.

Summary

We assessed the relationship between regional SM mass and bone mineral indices, and whether BMC normalized to site-matched SM mass differed with age. This cross-sectional study concluded that whole-body and regional SM mass are associated with site-matched BMD and BMC in both young and postmenopausal women. Moreover, the age-related differences in BMC were found to be independent of the ageing of SM mass in the arm and trunk region. However, differences in BMC measures of the leg and whole body were found to correspond to age-related decline of SM mass in postmenopausal women. These results support that the preservation of ageing of SM mass is an important factor for maintenance of leg and whole-body BMC especially in older women.

Acknowledgements

We gratefully acknowledge the dedicated women who participated in this project. We are also grateful for the technical support provided by Ms Naeko Kurose, and Ms Yumi Omori (National Institute of Health and Nutrition). This study was partly supported by 'Establishment of Consolidated Research Institute for Advanced Science and Medical Care,' Encouraging Development Strategic Research Centers Program, Special Coordination Funds for Promoting Science and Technology, Ministry of Education, Culture, Sports, Science and Technology, Japan, a grant from the ministry of Health, Labor and Welfare of Japan.

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European Journal of Clinical Nutrition (2009) 63, 529–535
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www.nature.com/ejcn

ORIGINAL ARTICLE

Resting energy expenditure can be assessed by dual-energy X-ray absorptiometry in women regardless of age and fitness

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Objective: To evaluate the possibility that measurement of the magnitude and distribution of fundamental somatic heat-producing units using dual-energy X-ray absorptiometry (DXA) can be used to estimate resting energy expenditure (REE) in both young and elderly women with different aerobic fitness levels.
Subjects and methods: Peak oxygen uptake (VO_2 peak) and REE_m were directly measured in 116 young (age: 22.3 ± 2.1 years) and 72 elderly (63.3 ± 6.4 years) women. The subjects were divided into four groups according to categories of age and VO_2 peak; young: high fitness (YH, $n=58$); low fitness (YL, $n=58$); elderly: high fitness (EH, $n=37$) and low fitness (EL, $n=35$). Using DXA, systemic and regional body compositions were measured, and REE_e was estimated from the sum of tissue organ weights multiplied by corresponding metabolic rate.
Results: Although there were remarkable differences in systemic and regional body compositions, no significant differences were observed between REE_m and REE_e in the four groups. REE_e significantly correlated with REE_m in elderly as well as young women; the slopes and intercepts of the two regression lines were statistically not different between the elderly and young groups (elderly: $y=0.60x+472$, $r=0.667$; young: $y=0.78x+250$, $r=0.798$; $P<0.001$, respectively). A Bland–Altman analysis did not indicate bias in calculation of REE for all the subjects.
Conclusion: These results suggest that REE can be estimated from tissue organ components in women regardless of age and aerobic fitness.

European Journal of Clinical Nutrition (2009) **63,** 529–535; doi:10.1038/sj.ejcn.1602980; published online 20 February 2008

Keywords: resting energy expenditure; age; aerobic fitness; body composition; female adults

Introduction

Resting energy expenditure (REE) accounts for 60–80% of total daily energy expenditure and is the basis for estimating the energy requirement. In the field of energy metabolism, early investigators showed intense interest in establishing the determinant factors of REE (Cunningham, 1980, 1991; Nelson *et al.*, 1992). To date, some earlier studies demonstrated that body mass, especially fat-free mass (FFM), has been a useful candidate in estimating REE (Ravussin and Bogardus, 1989; Fukagawa *et al.*, 1990; Tataranni and Ravussin, 1995).

Changes in body weight (BW) including fat mass (FM) and FFM may be caused by various factors, such as biological aging, decreasing physical activity levels, nutritional status and health condition. Particularly in women, the menopause is also associated with increased body mass accompanied by elevated adiposity (Fukagawa *et al.*, 1990; Svendsen *et al.*, 1995; Guo *et al.*, 1999). Svendsen *et al.* (1995) have noted that postmenopausal women had significantly larger amounts of fat deposition, a higher abdominal fat distribution and lower lean tissue mass, including skeletal muscle, bone and intestinal organs than premenopausal women.

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Received 16 July 2007; revised 5 October 2007; accepted 22 November 2007; published online 20 February 2008

Very little is known as to whether aerobically higher fitness individuals have higher metabolic rates in resting state. Ravussin and Bogardus (1989) reported that maximal O_2 uptake was not related to resting metabolic rate in non-diabetic, non-trained Pima Indians. However, they demonstrated that resting metabolic rate was significantly higher in well-trained men, when compared with sedentary men matched for BW, FFM and age (Ravussin and Bogardus, 1989). Thus, the question whether aerobic fitness level relates to REE remains unanswered.

Dual-energy X-ray absorptiometry (DXA) can easily and accurately assess the body composition, including bone mineral content (BMC), FM and FFM of the whole body and segments. Recently, Hayes *et al.* (2002) demonstrated that REE can be estimated from the summed heat productions from the weights of the brain, skeletal muscle mass (SM), adipose tissue (AT), bone and tissue organs by DXA. In view of the finding of Hayes *et al.* (2002), we decided to evaluate the possibility that measurement of the magnitude and distribution of fundamental somatic heat-producing units using DXA can be used to estimate REE in both young and elderly women with different aerobic fitness levels.

Materials and methods

Subjects

In total, 127 young women (age: 22.4 ± 2.2 years) and 83 elderly women (61.7 ± 8.1 years) were recruited for the study. Subjects who had too low and high body mass index (BMI <18.5 and BMI $>30\,\mathrm{kg\,m^{-2}}$) and had used medications that affect bone and estrogen replacement were eliminated from the analysis. Hence, 116 healthy young women (22.3 ± 2.1 years) and 72 healthy elderly women (63.3 ± 6.4 years) who had passed three years or more (13.5 ± 7.4 years) after menopause were selected for this study. The subjects were divided into four groups according to their aerobic fitness levels relative to BW (VO_2 peak: $\mathrm{ml\,kg^{-1}\,min^{-1}}$), and the median of VO_2 peak for each age, which were 36.4 (20–29 years), 27.1 (50–59 years), 25.8 (60–69 years) and 21.0 (70–79 years) $\mathrm{ml\,kg^{-1}\,min^{-1}}$ [young high fitness (YH): $n = 58$; young low fitness (YL): $n = 58$; elderly high fitness (EH): $n = 37$ and elderly low fitness (EL): $n = 35$]. All subjects were informed about the purpose and possible risks of the study and were then provided written informed consent, as approved by the Ethical Committee at the National Institute of Health and Nutrition in Japan.

Study protocol and direct measurement of REE

Participants came to the National Institute of Health and Nutrition in the morning. Subjects were asked to minimize any walking while en route from their home to the laboratory before REE determination. The subjects were restricted to perform any other exercises at least 24 h prior to the testing. The measured REEs (REE_m) was directly measured by open-circuit indirect calorimetry. Measurements were performed between 0700 and 0900 h after 10–12 h of fasting, except water, in a room at constant room temperature (23–25 °C). After entering the laboratory, subjects rested in the supine position for at least 30 min, and a Hans-Rudolph full face mask (Hans Rudolph Inc., Kansas City, MO, USA) was put on. Two samples of expired air were collected in Douglas bags for a duration of 10 min each, and the mean value was used for the analysis. For young subjects, all measurements were made during the follicular phase of the menstrual cycle.

An oxygen and carbon dioxide analyzer (Arco-1000A; Arco system, Japan) was used to analyze the rate of oxygen consumption and carbon dioxide production. The volume of expired air was determined using a dry gas volume meter (DC-5; Shinagawa, Japan) and converted to standard temperature, standard pressure and dry gas. Gas exchange results were converted to REE ($\mathrm{kcal\,day^{-1}}$) using Weir's equation (Weir, 1949).

Body composition analysis

Anthropometric measurements. BW was measured to the nearest 0.1 kg by using an electronic scale (Inner Scan BC-600; Tanita Co., Japan), and height was measured to the nearest 0.1 cm by using a stadiometer (YL-65; Yagami Inc., Japan). BW and height were measured with subjects wearing light clothing and no shoes. BMI was calculated by dividing BW in kilograms by the square of height in meters ($\mathrm{kg\,m^{-2}}$).

DXA. The percentage of fat (% body fat) and BMC of the whole body and appendicular lean soft tissue (LST) were measured by DXA (Hologic QDR-4500 DXA Scanner; Hologic Inc., Whaltham, MA, USA). Manufacturer's software version 11.2 for Windows was used to analyze the % body fat, BMC and LST. FFM and FM were calculated by BW and % body fat.

Test of aerobic capacity (VO_2 peak)

Young subjects were habituated to pedaling a dynamically calibrated Monark Model 828E cycle ergometer (Monark Exercise AB, Varberg, Sweden). On the other hand, aerobic capacity in elderly subjects was assessed by a progressive continuous test to exhaustion on a motor-driven treadmill with walking and running. All subjects wore a Hans-Rudolph full face mask. Oxygen consumption and carbon dioxide production of all subjects were measured during the last 30 s of each stage and analyzed using an oxygen and carbon dioxide analyzer. Heart rate was monitored electrocardiographically during the last 15 s of each minute, and a 'steady state' was regarded to have occurred if consecutive readings differed by <3 $\mathrm{beats\,min^{-1}}$. Four criteria were used to determine a successful maximal test: (1) a leveling or plateauing of VO_2 (defined as an increase in oxygen uptake $<2\,\mathrm{ml\,kg^{-1}\,min^{-1}}$); (2) maximal heart rate >195 or (220−age); (3) respiratory exchange ratio $\geqslant 1.0$ and (4) rating of perceived exertion ⩾18 (Johnson *et al.*, 2000; Santa-Clara *et al.*, 2006). VO2 peak was defined by the attainment of at least two of the four criteria.

Calculation of tissue organ mass and estimation of REE

Tissue organ mass was calculated using the previously reported prediction model as follows.

Bone mass (BM) was calculated by multiplying BMC times 1.85 (Snyder *et al.*, 1975; Heymsfield *et al.*, 1990). AT was assumed to be 85% fat (Heymsfield *et al.*, 2002), leading to the model based on FM. Thus, AT was calculated by multiplying FM times 1.18. SM was calculated using the prediction model of Kim *et al.* (2002) ($R^2=0.96$; SEE = 1.58 kg; $P<0.001$). Finally, residual mass (RM) was calculated as the difference between BW and the sum of the calculated BM, AT and SM.

$$\text{BM (kg)} = \text{BMC (g)} \times 1.85/1000$$

$$\text{AT (kg)} = \text{FM (kg)} \times 1.18$$

$$\text{SM (kg)} = 1.13 \times \text{LST (kg)} - 0.02 \times \text{age (years)} + 0.97$$

$$\text{RM (kg)} = \text{BW} - (\text{BM} + \text{AT} + \text{SM})$$

Estimation of REE (REE_e) was based on the sum of four body compartments (BM, AT, SM and RM) times the corresponding tissue respiration rate as follows. The specific resting metabolic rate of the four compartments was assumed from previously reported data, bone (2.3 kcal kg^{-1}), AT (4.5 kcal kg^{-1}), skeletal muscle (13 kcal kg^{-1}) and residual (53 kcal kg^{-1}) (Holliday *et al.*, 1967; Grande, 1989; Elia, 1992; Hayes *et al.*, 2002; Heymsfield *et al.*, 2002).

$$\text{REE}_e = 2.3\text{BM} + 4.5\text{AT} + 13\text{SM} + 53\text{RM}$$

Statistical analysis

The data were presented as mean ± s.d. Statistical analyses were carried out with the Sigma Stat 2.03 (Systat Software Inc., CA, USA). A two-way analysis of variance was used to test for interaction effects between the age and aerobic fitness levels among the mean values for the four groups. Where appropriate, the *Tukey* test was employed to locate the source of the significant differences. To determine the associations between measured and estimated REE, Bland–Altman plots were used (Bland and Altman, 1986). For all the statistical analyses, the level of significance was defined as less than 0.05.

Results

Table 1 presents the comparisons of characteristics, composition of whole body and aerobic fitness levels. BW and FFM were significantly higher in the YH group than in the YL group and EH group. The % body fat tended to be higher in the EL group compared with the other groups, but this interaction between age and aerobic fitness level was just short of statistical significance (age: $P<0.001$; aerobic fitness level: $P<0.001$; interaction: $P=0.056$). However, no significant interaction in BMI and FM was noted in the four groups.

REE_m in the YH group was ~15% higher than in the other three groups (Table 2).

Table 2 Measured and estimated resting energy expenditure

	Young		*Elderly*	
	YH (n = *58)*	*YL* (n = *58)*	*EH* (n = *37)*	*EL* (n = *35)*
REE_m	1265 ± 155	1118 ± 114^a	1080 ± 125^b	1093 ± 92
REE_e	1246 ± 161	1108 ± 101^a	1128 ± 108^a	1128 ± 89
$\text{REE}_m-\text{REE}_e$	19 ± 105	9 ± 89	−48 ± 92	−35 ± 79

Abbreviations: REE_m, measured by expiratory gas exchange; REE_e, estimated by four tissue organs.
Values are means ± s.d., kcal day^{-1}.
$\text{REE}_e = 13\text{SM} + 2.3\text{BM} + 4.5\text{AT} + 54\text{RM}$, significance was determined by two-way analysis of variance (ANOVA).
$^a P<0.05$ vs high-fitness group (same age group).
$^b P<0.05$ vs young group (same fitness category).

Table 1 Subject characteristics for the healthy female adults

	Young		*Elderly*	
	YH (n = 58)	*YL* (n = *58)*	*EH* (n = *37)*	*EL* (n = *35)*
Age (years)	21.8 ± 1.9	22.8 ± 2.2	62.4 ± 6.7	64.3 ± 6.1
Ht (cm)	163.2 ± 6.6	159.5 ± 6.3^a	153.1 ± 5.4^b	154.7 ± 5.0^b
BW (kg)	57.1 ± 6.8	53.9 ± 5.9^a	53.2 ± 6.0^b	55.5 ± 5.9
BMI (kg m ^{2})	21.4 ± 1.9	21.2 ± 1.9	22.7 ± 2.1	23.2 ± 2.5
FFM (kg)	44.7 ± 5.6	39.5 ± 4.0^a	37.6 ± 3.7^b	37.9 ± 3.3
FM (kg)	12.3 ± 2.6	14.3 ± 3.0	15.5 ± 3.6	17.7 ± 4.1
% body fat	21.6 ± 3.6	26.5 ± 3.6	29.0 ± 4.5	31.5 ± 4.8
VO_2 peak (ml kg ^{1} min ^{1})	42.3 ± 4.8	32.1 ± 2.9^a	29.8 ± 4.2^b	22.2 ± 2.8^{a,b}

Abbreviations: BMI, body mass index; BW, body weight; FFM, fat-free mass; FM, fat mass; Ht, height.
Values are means ± s.d.
Significance was determined by two-way analysis of variance (ANOVA).
$^a P<0.05$ vs high-fitness group (same age group).
$^b P<0.05$ vs young group (same fitness category).

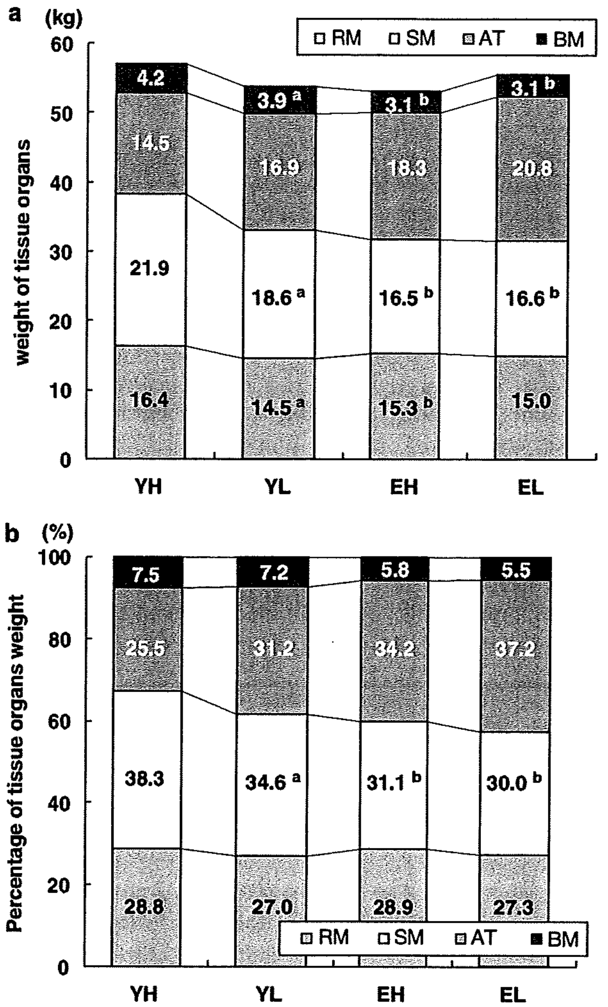

Figure 1 Four tissue organ components in women expressed as a weight (a) and as their respective fractional contributions to body weight (b). RM, residual mass; SM, skeletal muscle; AT, adipose tissue; BM, bone mass. Significance was determined by two-way analysis of variance (ANOVA). $^{a}P<0.05$ vs high-fitness group (same age group) and $^{b}P<0.05$ vs young group (same fitness category).

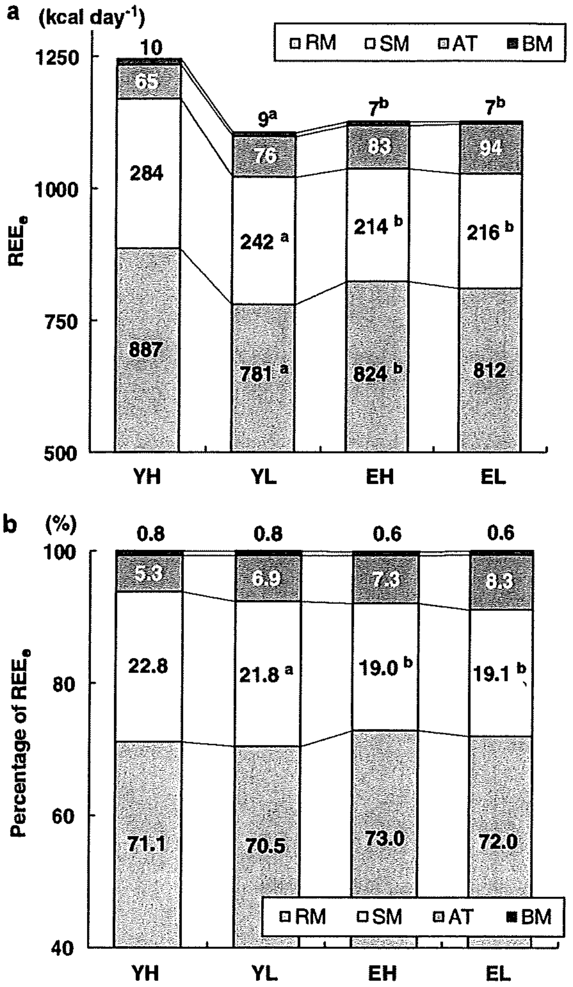

Figure 2 Four tissue organ components in women expressed as a specific energy expenditure (a) and as their respective fractional contributions to REE_e (b). RM, residual mass; SM, skeletal muscle; AT, adipose tissue; BM, bone mass; REE_e, resting energy expenditure estimated by four tissue organs. $REE_e = 13SM + 2.3BM + 4.5AT + 54RM$. Significance was determined by two-way analysis of variance (ANOVA). $^{a}P<0.05$ vs high-fitness group (same age group) and $^{b}P<0.05$ vs young group (same fitness category).

The absolute and relative values of the weight of the four tissue organs are presented in Figures 1a and b, respectively. SM and BM in YH were significantly higher than in YL, and were also significantly higher in young women than in elderly women of the same fitness category. The absolute value of RM was also significantly higher in YH than in YL and EH. However, no significant interaction in AT was noted among the four groups. When these four tissue masses were expressed as a percentage of BW, SM in YH was significantly higher than in YL, and was also significantly higher in young women than in elderly women of the same fitness category. This result was similar to that for SM mass. The relative mass of AT in EL tended to be higher than in the respective group, whereas no statistical significance in this interaction between age and aerobic fitness levels was observed.

Figures 2a and b present the absolute and relative values of the energy expenditure of the four different tissue organs. Our data noted significant differences in only SM as a percentage of the energy expenditure in the four groups. Specifically, the energy expenditure of SM as a percentage of the whole body in elderly women was lower than in the same fitness category (percentage energy expenditure of RM, AT and BM did not differ among the groups).

Tissue organ-derived REE_e was significantly higher in the YH than in the YL and EH groups (Table 2). There was also no

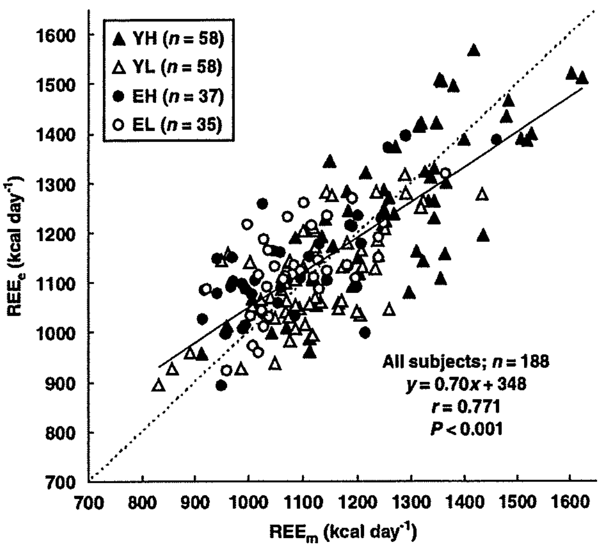

Figure 3 Relationship between the measured and estimated resting energy expenditure. $\mathrm{REE_m}$, measured by expiratory gas exchange; $\mathrm{REE_e}$, estimated by four tissue organs. $\mathrm{REE_e} = 13SM + 2.3BM + 4.5AT + 54RM$.

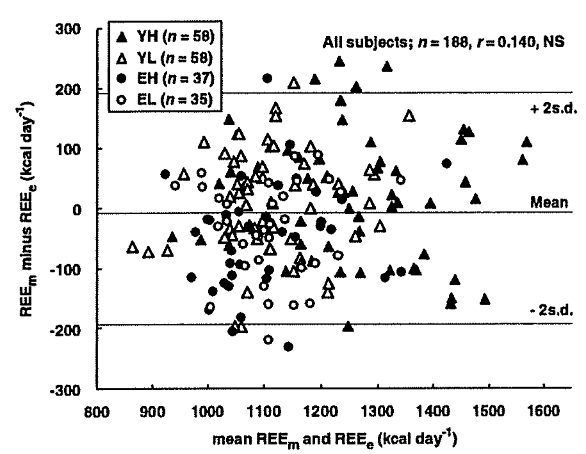

Figure 4 Bland–Altman analysis. Plots of the differences between $\mathrm{REE_m}$ and $\mathrm{REE_e}$. $\mathrm{REE_m}$, measured by expiratory gas exchange; $\mathrm{REE_e}$, estimated by four tissue organs. $\mathrm{REE_e} = 13SM + 2.3BM + 4.5AT + 54RM$.

significant difference between $\mathrm{REE_m}$ and $\mathrm{REE_e}$ in the four groups. In addition, a significant relationship between $\mathrm{REE_m}$ and $\mathrm{REE_e}$ was observed in all subjects (Figure 3). A Bland–Altman analysis did not indicate any bias in the calculation of REE for all subjects (Figure 4).

Discussion

The major finding from the present study is that REE in adult women can be accurately estimated from tissue organ components by using DXA regardless of age and aerobic fitness levels.

Measured and estimated REEs

A strongly significant relationship between $\mathrm{REE_m}$ and $\mathrm{REE_e}$ was observed in all subjects ($r = 0.771$, $P < 0.001$; Figure 3) and a Bland–Altman analysis did not indicate bias in the estimation of REE (all subjects: $r = 0.140$; young: $r = 0.041$; elderly: $r = 0.133$, NS, respectively; Figure 4). Furthermore, our study indicated that $\mathrm{REE_e}$ was related significantly to $\mathrm{REE_m}$ in both young and elderly women (elderly: $y = 0.60x + 472$, $r = 0.667$; young: $y = 0.78x + 250$, $r = 0.798$; $P < 0.001$ for both), and the slopes and intercepts of the two regression lines were statistically not different between the young and elderly groups (slopes: $t = 1.652$; intercept: $t = 1.881$; NS for both). This suggests the possibility that the difference in the ratio of SM and RM to FFM is important rather than the decline in the specific metabolic rate with advancing age.

It is well known that REE decreases after menopause in women, potentially contributing to changes in body composition (Vaughan *et al.*, 1991; Hunter *et al.*, 2001). It is unclear, however, whether the decrease in REE is a consequence of an age-dependent decrease in FFM, which includes skeletal muscle, bone and tissue organs. In the present study, the absolute $\mathrm{REE_m}$s (kcal day^{-1}) are ~15% lower in the YL, EH and EL groups compared with the YH group (Table 2). When $\mathrm{REE_m}$ is expressed in terms of FFM, however, no significant differences in absolute $\mathrm{REE_m}$ were obtained among the groups (YH vs YL vs EH vs EL: 28.4 ± 2.3 vs 28.4 ± 2.3 vs 28.8 ± 2.7 vs 29.0 ± 2.1 kcal kg^{-1} day^{-1}). This result did not correspond to previous reports on sedentary adult women and men (Van Pelt *et al.*, 1997, 2001; Piers *et al.*, 1998). Van Pelt *et al.* (1997, 2001) and Piers *et al.* (1998) reported that the effect of age on REE was significantly negative in healthy sedentary adults, even after adjusting for age-related differences in body composition.

On the basis of the different tissue masses and their specific metabolic rates (Elia, 1992), Gallagher *et al.* (1998, 2000) examined the relationship between REE and body composition divided into numerous tissues and organs. In addition, Hayes *et al.* (2002) investigated whether the REE can be calculated from the summed heat productions from the weight of tissue organs estimated by DXA. Their study showed that no bias was detected between measured and predicted REEs (Hayes *et al.*, 2002).

Aerobic fitness level and body composition

Our present data showed that the aerobic fitness level in the elderly was ~30% lower than in young adults in both high- and low-fitness level groups. The reduction rate of $\mathrm{VO_2}$ peak/BW was ~7.5% per decade of age. Earlier study showed a 7.5% reduction per decade in $\mathrm{VO_2}$ max for 20–75 years of age (Pollock *et al.*, 1987).

In the present study, the % body fat in high fitness or young group was lower than in low fitness or elderly group of the same category, but this interaction between age and aerobic fitness level was just short of statistical significance ($P = 0.056$). On the other hand, FFM was significantly higher in YH than in the other three groups, and no significant differences in FFM were noted among the YL, EH and EL groups (Table 1). These findings are in accordance with earlier studies (Van Pelt *et al.*, 1997, 2001), suggesting that keeping aerobically fit can prevent an increase in % body fat with aging.

Our present study also focused on the weight or energy expenditure of DXA-estimated tissue organs, as a component of the whole body, to assess the relationship between FFM and $\mathrm{REE_m}$. The percentage of AT mass suggested that keeping a high aerobic fitness level may suppress the age-related increase in total body fat. In contrast, SM decreases in elderly women regardless of their aerobic fitness levels (Figures 1a and b). These results suggested that, in elderly women, it could be difficult to prevent a decrease in the volume of skeletal muscle, by performing aerobic exercise, such as swimming, walking or jogging. Resistance exercise should be combined with aerobic exercise for elderly women.

Limitations

Our investigation has a few limitations. First, the weight of tissue organs could not be directly measured by using apparatus, such as a magnetic resonance imaging. Second, we did not observe directly the magnitude of the summed heat produced by the tissue organs. Third, we did not test middle-aged (30–49 years) adults. Future studies should widen the characteristics of the subjects to include lean and obese adults or middle-aged adults. Future studies are needed to extend these observations and to analyze gender-related, hormonal, ethnic and other determinant factors of REE.

In conclusion, the present investigation demonstrated that estimation of the four tissue organs by using DXA allows successful calculation of REE in female adults regardless of age and aerobic fitness levels. The findings suggest the possibility that REE is regulated mainly by the mass of the tissue organs with lower and higher metabolic rates, including skeletal muscle and intestinal organs, rather than a decline in the specific metabolic rate of different tissue organs associated with advancing age and decreasing aerobic fitness levels in young and elderly women.

Acknowledgements

We express our appreciation to the subjects for their cooperation in this study. We thank the members of the National Institute of Health and Nutrition for their help in this experiment. This study was supported by a Research Grant for Academic Frontier Projects from the Ministry of Education, Culture, Sports, Science and Technology (05F-02), a Waseda University Grant for Special Research Projects (2005A-932, 2006B-242), Health Sciences Research Grants from the Ministry of Health, Labor and Welfare, Medical Health Care Research Grants from the Consolidated Research Institute for Advanced Science and Medical Care at Waseda University and Research Grants from the Japanese Olympic Committee.

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原　著

全身持久力の向上とメタボリックシンドローム改善効果

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(平成20年7月7日受理)

要旨：全身持久力の代表的な指標で、安全に測定できる換気性閾値を用いて、全身持久力の向上とメタボリックシンドローム改善との関係を日本人男性で検討した。対象は当施設において、1年間隔で2度呼気ガス分析法による換気閾値の測定、空腹時採血を受け、薬物治療を受けていない男性70名(45.9±7.7歳)であった。測定項目は、換気性閾値に加え、身長、体重、腹囲、ヒップ囲、安静時血圧、中性脂肪、HDLコレステロール、空腹時血糖であった。メタボリックシンドロームの診断はわが国の診断基準を用いた。2回目の受診では、体重、腹囲、血圧、中性脂肪の有意な改善が認められた。換気性閾値の増加した群(I群)と増加しなかった群(II群)の2群で比較すると、I群ではメタボリックシンドロームが改善した頻度が高く、腹囲、HDLコレステロールが有意に改善した。換気性閾値時酸素摂取量の向上とメタボリックシンドロームの改善との間には有意な関連が認められ、運動習慣の獲得等をとおして全身持久力の向上をはかることが、メタボリックシンドローム予防、改善に必要と思われた。

(日本予防医学会雑誌 2009, 4: 11-16)

—キーワード—
メタボリックシンドローム, 換気性閾値, 酸素摂取量

Introduction

Metabolic syndrome is a common disorder and has become a public health challenge in Japan [1]. For example, 30.7% of men and 3.6% of women have been diagnosed as having metabolic syndrome using the new criterion developed in Japan [2]. Metabolic syndrome has been associated with an increased risk of cardiovascular disease [3], proteinuria [4], and elevation of hepatic enzymes [5]. Lifestyle modifications, especially exercise, are important for preventing and improving metabolic syndrome.

Although maximum oxygen uptake is generally considered an accurate and reliable parameter, it is not fully applicable to the population in clinical practice. Ventilatory threshold (VT) is closely linked to maximum oxygen uptake. It is defined as the upper limit of aerobic exercise and is also thought to serve as an accurate and reliable standard for exercise prescription [6]. Since exercise intensity at VT is not harmful to cardiovascular function, it can be safely applied to patients with myocardial infarction as exercise prescription [7]. We have previously reported in a cross-sectional study that lower levels of oxygen uptake at VT were characteristic in subjects with metabolic syndrome [8]. However, whether an increase in oxygen uptake at VT is beneficial for improving metabolic syndrome, and what effects this will have on metabolic syndrome remain to be investigated in a longitudinal study.

In this study, we evaluate the link between increases in oxygen uptake at VT and metabolic syndrome in Japanese men with a 1-year follow up.

Subjects and Methods

Subjects. We used data for 70 (0.5%) Japanese men, aged 45.9±7.7 years, retrospectively from a database of 14,345 subjects who met the following criteria: (1) received an annual health check-up at baseline from June 1997 to March 2006, (2) received an annual health check-up every year with a follow up duration of 1-year, (3) received anthropometric and oxygen uptake at VT measurements, fasting blood examination and blood pressure measurements as part of the annual health check-up, (4) received no medications for diabetes, hypertension, and/or dyslipidemia, and (5) provided written informed consent (Table 1).

Table 1: Clinical profiles and changes in parameters with 1-year follow up

	Baseline	Follow up	p
Number of subjects	70		
Height (cm)	165.4 ± 4.9		
Body weight (kg)	81.3 ± 8.4	78.7 ± 9.0	<0.0001
Abdominal circumference (cm)	93.9 ± 8.0	90.9 ± 8.5	<0.0001
Oxygen uptake at ventilatory threshold (ml/kg/min)	14.5 ± 2.6	14.8 ± 2.8	0.8037
Work rate at ventilatory threshold (W)	85.1 ± 15.0	85.9 ± 15.7	0.2709
Heart rate at ventilatory threshold (beats/min)	103.1 ± 10.4	100.1 ± 10.6	0.0050
Systolic blood pressure (mmHg)	132.9 ± 14.8	126.4 ± 12.2	<0.0001
Diastolic blood pressure (mmHg)	83.6 ± 12.4	76.2 ± 8.5	<0.0001
Triglyceride (mg/dl)	165.7 ± 102.4	128.5 ± 73.9	0.0010
HDL cholesterol (mg/dl)	52.1 ± 14.3	53.3 ± 13.8	0.1352
Blood sugar (mg/dl)	106.4 ± 23.2	110.3 ± 35.1	0.5474

Mean ± SD

At the first annual health check-up, all subjects were given instructions by well-trained medical staff on how to change their lifestyle *i.e.* not to eat too much, consider balance when they eat and increase their daily steps.

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

Anthropometric and body composition measurements. Anthropometric and body compositions were evaluated based on the following parameters: height, body weight and abdominal circumference. Body mass index (BMI) was calculated by weight / [height] ^{2} (kg/m^2). Abdominal circumference was measured at the umbilical level in standing subjects after normal expiration [1].

Blood pressure measurements at rest. Resting systolic and diastolic blood pressure were measured indirectly using a mercury sphygmomanometer placed on the right arm of the seated participant after at least 15 minutes of rest.

Blood sampling and assays. Overnight fasting serum levels of high density lipoprotein (HDL) cholesterol, triglycerides (L Type Wako Triglyceride・H, Wako Chemical, Osaka) and plasma glucose were measured.

Definition of metabolic syndrome. Men with a waist circumference in excess of 85 cm were defined as having metabolic syndrome if they also had two or more of the following components: 1) Dyslipidemia: triglycerides≧150 mg/dl and/or HDL cholesterol<40 mg/dl, 2) High blood pressure: blood pressure≧130/85 mmHg, 3) Impaired glucose tolerance: fasting plasma glucose≧110 mg/dl [1].

Exercise testing. A graded ergometer exercise protocol [9] was performed. Two hours after breakfast, a resting ECG was recorded and blood pressure was measured. Then, all participants were given graded exercise after 3 min of pedaling on an unloaded bicycle ergometer (Excalibur V2.0, Lode BV, Groningen, Netherlands). The profile of incremental workloads was automatically defined by the methods of Jones [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 the recording of heart rate (HR). Expired 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., Netherlands). VT was determined by the standard of Wasserman et al [6], 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, $\dot{V}O_2$ (ml/kg/min), work rate (W), and heart rate (beats / min) were measured and recorded.

Statistical analysis. All data are expressed as mean ± standard deviation (SD) values. A statistical analysis was performed using a paired *t* test, an unpaired *t* test and χ^2 test: $p<0.05$ was considered to be statistically significant. Pearson's correlation coefficients were calculated and used to test the significance of the linear relationship among continuous variables.

Results

The clinical parameters at the baseline and the 1-year follow up are summarized in Table 1. Anthropometric and body composition parameters such as body weight and abdominal circumference were significantly reduced after one year. Systolic blood pressure, diastolic blood pressure, triglyceride levels and heart rate at VT were significantly reduced. The prevalence of metabolic syndrome was also significantly reduced (Baseline: 31 men. Follow up: 24 men) (Table 2).

Table 2: Changes in the prevalence of metabolic syndrome

	Metabolic syndrome (Follow up)		
Metabolic syndrome (Baseline)	(-)	(+)	p
(-)	34	5	<0.0001
(+)	12	19	

Thirty five men unexpectedly increased their oxygen uptake at VT by the time of the 1-year follow up. We investigated the changes in the prevalence of metabolic syndrome amongst men who had different levels of increased oxygen uptake at VT [Group I: Delta (delta represents positive changes in parameters) oxygen uptake at VT ≧ 0 ml/kg/min, Group D: Delta oxygen uptake at VT < 0 ml/kg/min] (Table 3). The prevalence of subjects with metabolic syndrome at baseline and without metabolic syndrome at follow up was higher (8 men, 22.9%) in Group I than those in Group D (4 men, 11.4%).