も約 8,000 歩／日を示した。40歳代、50歳代、60歳代の平均歩数は、男性;8,189 歩、8,310 歩、7,806 歩、女性;8,177 歩、8,302 歩、7,495 歩であった(表2)。

3. 週当たりのメッツ・時推定値ついて

歩数の解析同様に 1 日 8 時間未満のデータは除外した。ライフコーダ強度 3 以上(2.9 メッツに相当)の記録をもとに算出した全体の平均値は 13.8 メッツ・時/週であり、女性(12.8 メッツ・時/週)に比べ男性(15.2 メッツ・時/週)で高値を示した。40 歳代及び 50 歳代の男女別の平均値の差は約2メッツ・時/週、60 歳代別では3メッツ・時/週であった(表2)。

4. 1 日の平均歩数と週当たりのメッツ・時推定値の関係について

1 日の平均歩数と週当たりのメッツ・時推定値の関係を図1に示した。得られた 2 次回帰式より平均 1 日 1 万歩に相当する週当たりのメッツ・時推定値は約18メッツ・時/週を示し、1 万 2 千歩では約23メッツ・時/週となった。

23メッツ・時/週に相当する歩数について、男女別に見た概算値では、男性:11,500 歩、女性 12,500 歩であった。また、40 歳代、50 歳代、60 歳代別にそれぞれの 2 次回帰曲線より概算したところ、40 歳代:12,500 歩、50 歳代:12,800 歩、60 歳代:11,500 歩であった。

5. 週当たりのメッツ・時推定値別にみた肥満リスクについて

週当たりのメッツ・時推定値結果に基づき最も低い水準を Q1 とし5群に分類した(図2)。各群の範囲はQ1(n=1046):～6.6 メッツ・時/週、Q2(n=1047):6.6～10.0 メッツ・時/週、Q3(n=1047):10.0～13.8 メッツ・時/週、Q4(n=1047):13.8 ～ 19.4 メッツ・時/週、Q5(n=1047):19.4～メッツ・時/週であった。

肥満リスク(BMI25 以上)に対する性・年齢による調整オッズ比は、Q1を基準に Q2で有意な低値を示し($p<0.01$)、Q2から Q5までほぼ同水準であった。

D. 考察

様々な日常生活活動をライフコーダで感知するには限界がある。例えば、活動により位置エネルギーの変化がある階段昇降、水泳など機器を装着して活動できない運動などである。また、今回の解析にはライフコーダ強度3以上の身体活動を推定値の算出に用いたが、健康づくりのための運動指針 2006 に掲げられている 3 メッツ以上の身体活動と同義的に取り扱うことに対しては慎重であるべきと考える。以上のような限界を含めた上で、週当たりのメッツ・時推定値と肥満との関連性を検討した。

平成 16 年の国民健康・栄養調査によると、BMI25 以上である男性は 40 歳代では 32.7%、50 歳代では 30.8%、60 歳代では 29.7%と報告されている。今回の調査対象者は、研究協力への同意が得られた集団であるため無作為抽出データではないものの、国の調査結果とほぼ同じであった。一方、女性については 40 歳代では 17.9%、50 歳代では 24.1%、60 歳代では 29.9%と報告されており、いずれの年代も今回の調査対象者の方が低値を示す傾向が認められた。

週当たりのメッツ・時推定値に基づき最も低

い水準から 5 群に分類し肥満度リスクを検討した。その結果、最も低い水準(Q1 群)を基準として 2 番目に低い水準(Q2 群)以上のすべての群において有意なリスク低下を認めた。Q2 群の週当たりのメッツ・時推定値の範囲は、ほぼ 7～10 メッツ・時/週に相当する。このような低い水準に対する増加でさえ有意な肥満度リスク低下が認められたことは、日常生活活動に 3 メッツ以上の生活活動あるいは運動を少しでも取り入れることで効果が期待できることを示唆している。さらに、Q3 群の点推定値 0.61(0.49-0.74)は Q5 群の 0.59 (0.48-0.72)のそれとほぼ同水準であることから、肥満予防のための目標身体活動レベルは Q3 群の最低範囲である 10 メッツ・時/週以上が妥当であるかもしれない。健康づくりのための運動指針 2006 作成に用いられたシステマティックレビューによると、肥満をエンドポイントとする研究では5メッツ・時/週未満では効果が認められず、5～13メッツ・時/週まではレビューの条件を満たした研究がなく、14メッツ・時/週以上で初めて効果を認める研究が存在する。今回我々の研究結果は、今までの研究結果よりさらに低い水準での肥満予防効果を見出した研究といえる。ただし、これらの数値については本解析の定義として用いた強度設定の問題や日常生活活動をすべて把握していない点などを考慮しなければならない課題は残る。

様々な限界点は存在するものの広く国民に対してわかりやすい指標の提示は必要と思われる。そこで、今まで広く活用されてきた歩数との関係を検討した。歩数は量的な指標であり活動強度レベルを含んでいないため、強度と量を合わせて評価するメッツ・時で示す身体活動量とは異なるものであるが、図1のように両者の間には非常に高い相関関係が認められた。そこで、23(メッツ・時/週)に相当する歩数を概算したところ、約 12,000 歩に相当する水準であった。男女別に見た概算値では、男性:11,500 歩、女性 12,500 歩であり、日常行動の活動内容や活動強度が異なることが要因であると思われる。

E. 結論

地域住民 5,234 名を対象とした横断的研究結果より、3 メッツ以上の身体活動の増加が低い水準での変化であっても肥満予防の効果が期待でき、肥満予防に有効と考えられる身体活動量は 7 メッツ・時/週以上であり、目標とする身体活動レベルは 10 メッツ・時/週以上が妥当であることが示唆された。

F.健康危険情報

問題なし。

G.研究発表

1. 論文発表

なし

2. 学会発表

なし

H.知的財産権の出願・登録状況

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

表1. 対象者の特性

	男	女
n	2216	3018
年齢（才）	57.2 ± 8.2	56.3 ± 8.2
身長（cm）	166.6 ± 6.1	154.2 ± 5.5
体重（kg）	66.0 ± 9.7	53.6 ± 7.9
BMI (kg/m^2)	23.7 ± 3.0	22.5 ± 3.2
1日の平均歩数（歩／日）	8060 ± 3651	7945 ± 2986
週当たりの身体活動量(メッツ・時/週)[1)]	15.2 ± 10.5	12.8 ± 7.9
装着日数（日／10日）	9.0 ± 1.9	9.5 ± 1.3

平均値±標準偏差

1) ライフコーダ記録より3メッツ以上に相当する身体活動量を推定値として算出

表2. 性別、年代別の対象者の特性

年代	性	n.	BMI (kg/m^2)	1日の平均歩数（歩/日）	週当たりの身体活動量（メッツ・時/週）
40歳代	男	439	24.0 ± 3.3	8189 ± 3475	15.4 ± 8.8
	女	717	21.9 ± 3.2 **	8177 ± 2901	13.4 ± 7.1 **
50歳代	男	781	23.7 ± 3.1	8310 ± 3646	15.5 ± 9.7
	女	1076	22.5 ± 3.1 **	8302 ± 3040	13.5 ± 7.9 **
60歳代	男	996	23.6 ± 2.9	7806 ± 3717	14.9 ± 11.8
	女	1225	23.0 ± 3.2 **	7495 ± 2930 *	11.9 ± 8.3 **

平均値±標準偏差

*; $p<0.05$ vs 男、**; $p<0.01$ vs 男

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研究事業）

分担研究報告書

運動が骨代謝に及ぼす影響に関する研究

分担研究者：戸山　芳昭　慶應義塾大学医学部整形外科　教授

研究要旨：自然発症型糖尿病(GK/Jcl)ラットを用いて、運動、活性型ビタミンD3、副甲状腺ホルモンが骨代謝に及ぼす影響を検討した。そのうち副甲状腺ホルモンは、骨形成を強く促進し代謝回転を亢進させることで、Ⅱ型糖尿病モデルラットの骨塩量・骨強度を効果的に改善することを明らかにした。

A. 研究目的

自然発症型糖尿病ラット（GK/Jcl）を用いて、走行運動、ビタミンD 、PTHが骨代謝に及ぼす影響を検討し、生活習慣病をともなう続発性骨粗鬆症に対する作用メカニズムを明らかにすることを目的とした。

B. 研究方法

23週齢のGK/Jcl雄性ラット32匹を無治療群（NT群）、運動群（Ex群）、活性型ビタミンD3投与群（ALF群）、副甲状腺ホルモン投与群（PTH群）の4群に分けた。Ex群では小動物用トレッドミル装置を用いた走行運動を走行速度12m/分、60分間/日、週5日間行った。ALF群ではalfacalcidol 0.1μg/kg, 連日経口投与した。PTH群ではPTH(1-34) 50μg/kgを1日おきに皮下注射した。運動開始12週後に屠殺し、腰椎と大腿骨の骨密度（BMD）を測定した。また腰椎では圧迫試験、大腿骨中央部では3点折り曲げ強度試験による最大破断強度を求めた。また血清Ca、P、オステオカルシン（OC）尿中デオキシピリジノリン(D-Pyr)を測定した。

（倫理面への配慮）

ラットを用いる実験に関しては、慶應義塾大学の実験動物に関する規則に則って計画し、遂行した。

C. 研究結果

Ex群の体重はNT群、ALF群、PTH群より減少していた。NT群とALF群、PTH群との間には有意な体重差はなかった。血糖値は、Ex群のみ200mg/dl に低下しており、そのほかの群は250から300mg/dl を推移していた。骨代謝マーカーについては、NT群に対してEx群ではOCが5.7%増加しD-Pyr が8.6%減少し、ALF群ではOCが5%増加、D-Pyr が23%減少した。PTH群ではOCが70%増加し、D-Pyrが10%増加した。

腰椎のBMDはNT群に対して運動群で3%、ALF群で12%、PTH群で10%それぞれ増加した。圧縮強度試験ではNT群に対してEx群で18%、ALF群で25%、PTH群で70%それぞれ増加した。大腿骨骨幹部のBMDはPTH群でのみ非治療群に対して4%の増加を認めた。３点折り曲げ強度試験による大腿骨骨幹部最大破断強度ではPTH

群で非治療群に対して9%の増加が見られた。

D. 考察

糖尿病の慢性合併症としての骨代謝異常については、特にⅠ型糖尿病（IDDM）では低代謝回転型骨粗鬆症の頻度が高いといわれているが、Ⅱ型糖尿病（NIDDM）では多くの交絡因子が関与するため一定の見解は得られていない。今回、Ⅱ型糖尿病のモデルとして知られるGK/Jcl雄性ラットを用いた解析の結果、運動群・ビタミンD投与群・PTH群のなかで、骨塩量と骨質の改善に最も有効なのは、PTH群であることが明らかになった。PTHは海綿骨の骨量増加効果が大きく、皮質骨の骨量を減少させるという報告がある。本研究でもPTH群では腰椎のBMDは10%増加、大腿骨骨幹部は7%の増加を認め、海綿骨領域の多い腰椎部により大きい効果があったと思われる。また、PTH群では血清オステオカルシンが有意に増加し、骨塩量と骨強度を増加させたことから、ほかの介入群とは異なり、骨形成促進という作用メカニズムを介して、II型糖尿病モデルラットの骨質を効果的に改善することが示唆された。

E. 結論

走行運動、ビタミンD、PTHは、Ⅱ型糖尿病のモデルラットにおいて腰椎の骨塩量を増加させた。なかでもPTHは骨形成を強く促進し、代謝回転を高めることで骨質を改善し、Ⅱ型糖尿病をともなう骨粗鬆症患者の骨折リスクを減少させる可能性がある。

F. 健康危険情報

問題なし。

G. 研究発表

1. 論文発表

なし

2. 学会発表

骨形態計測学会. 2005年7月

H. 知的財産権の出願・登録状況

なし

別紙４

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
なし							

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Sanada K、Kuchiki T, Miyachi M, McGrath K, Higuchi M、Ebashi H	Effects of age on ventilatory threshold and peak oxygen uptake normalised for regional skeletal muscle mass in Japanese men and women aged 20- 80 years.	European Journal of Applied Physiology:	99巻５号	475－483	2007
kawano H, Tanaka H, Miyachi M	Resistance Training and Arterial Compliance: Keeping the Benefits While Minimizing the Stiffening	Journal of Hypertension	24巻９号	1753－1759	2006
Wu J, Oka J, Tabata I, Higuchi M, Toda T, Fuku N, Ezaki J, Sugiyama F, Uchiyama S, Yamada K, Ishimi Y	Effects of isoflavone and exercise on bone and lipid metabolism in postmenopausal Japanese women: One- year randomized placebo-controlled trial	Journal of Bone and Mineral Research	21 巻	780－789	2006
山本英彦，武友麻衣，田中宏暁，田中宏暁，吉田るみ子，萱島誠，小野敦子，名取省一，橋口照人，丸山征郎	生活習慣病の予防・改善のための運動療法－ベンチステップ運動を用いた無作為化比較試験	人間ドック	21巻４号	18－23	2006

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ORIGINAL ARTICLE

Effects of age on ventilatory threshold and peak oxygen uptake normalised for regional skeletal muscle mass in Japanese men and women aged 20–80 years

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Abstract Ventilatory threshold (VT) is an important predictor of cardiorespiratory fitness, such as peak oxygen uptake ($\dot{V}_{O_2peak}$), and is a valuable index of aerobic exercise intensity. However, little is known about the role of skeletal muscle (SM) mass in the age-associated decline of VT. Therefore, the present study was performed to investigate the effects of age on cardiopulmonary fitness normalised for regional SM mass in 1,463 Japanese men and women, and to determine the relevance of VT normalised to SM mass based on age and gender. Total, trunk and thigh SM mass were measured using an ultrasound method, while $\dot{V}_{O_2peak}$ and VT were determined during treadmill walking. $\dot{V}_{O_2peak}$ was estimated using the predicted maximum heart rate (HR) and the HR-$\dot{V}_{O_2}$ relationship for sub-maximal treadmill walking. There were significant negative correlations between VT normalised for body mass and age in men and women ($P < 0.001$). Age-associated declines were also observed in VT normalised for body mass in both men and women; however, VT normalised for SM mass was not significantly different with age. Significant correlations were also observed between thigh SM mass and VT in both men and women. These results suggest that thigh SM mass is closely associated with $\dot{V}_{O_2peak}$ and/or VT in both men and women, and the decrease in VT with age is predominantly due to an age-related decline of SM mass. Moreover, this study provides normative cardiorespiratory fitness data regarding VT normalised SM mass in healthy men and women aged 20–80 years.

Keywords Age · Anaerobic threshold · Gender · Skeletal muscle mass · Ultrasound · $\dot{V}_{O_2peak}$

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Introduction

Low levels of cardiorespiratory fitness, such as peak oxygen uptake ($\dot{V}_{O_2peak}$), are risk factors for future cardiovascular mortality, as well as mortality of all causes in middle-aged and elderly men and women (Blair et al. 1995, 1989; Fletcher et al. 1996). Although measurement of $\dot{V}_{O_2peak}$ is important to classify an individual's health risk, the accurate determination of $\dot{V}_{O_2peak}$ requires a maximum graded exercise test (GXT) performed on a treadmill or cycle ergometer. However, GXT are accompanied by a certain degree

of risk, such as myocardial infarction, and the need to consider the subject's motivation even in healthy middle-aged and older individuals (American College of Sports Medicine 1995). Therefore, predicted maximal heart rates (HR), such as 220 minus age, are commonly used to estimate $\dot{V}_{O_2peak}$ using the HR-$\dot{V}_{O_2}$ relationship during sub-maximal exercise (McArdle 2001). The ventilatory threshold (VT) has been defined as the point when the changes in ventilation (VE) are disproportionately greater than the changes in $\dot{V}_{O_2}$ with increasing workloads which occurs at the lactate acidosis threshold (Wasserman et al. 2005). The VT can be used directly and accurately as a measure of cardiorespiratory fitness (Gaskill et al. 2001), and is also useful for evaluating the training effect in low to moderate intensity physical exercise (Zhang et al. 2003). Furthermore, it has been shown that the changes in VT in low to moderate exercise are associated with cardiac autonomic nervous function, which may be used clinically as a predictor of cardiovascular morbidity and mortality (Tuomainen et al. 2005). Thus, when studying the effects of aging on cardiorespiratory fitness, both $\dot{V}_{O_2peak}$ and VT are key factors.

The age-related decline of $\dot{V}_{O_2peak}$ has been attributed to changes in body composition, especially a loss of skeletal muscle (SM) mass, or sarcopenia (Fleg and Lakatta 1988; Frontera et al. 2000; Proctor and Joyner 1997). SM mass is important for understanding the decline in $\dot{V}_{O_2peak}$ with age, because the arterial–venous difference for oxygen in SM is one of the determinant factors of $\dot{V}_{O_2peak}$ according to the Fick principle. Previously, we reported that lower body SM mass measured by magnetic resonance imaging (MRI) was strongly correlated with $\dot{V}_{O_2peak}$ during running (Sanada et al. 2005), independent of body mass and fat-free body mass (FFM). However, to our knowledge, there is no evidence supporting the relationship between VT and total or regional SM mass as a function of age in a large population. Therefore, it is necessary to clarify what factors are important for normalisation (i.e., body mass, FFM, SM mass) in order to accurately evaluate VT.

It is difficult to accurately quantify total and regional SM mass because it requires the use of MRI or computerised tomography (the gold standard), which are costly and time-consuming for analysis. Recently, our laboratory developed several regression-based prediction equations (Sanada et al. 2006) of SM mass based on B-mode ultrasound of muscle thickness (MTH). We have further demonstrated that use of these equations are a valid method for predicting SM mass in healthy Japanese adults, and a viable alternative to costly MRI measurements. Ultrasound has been widely employed for measuring SM size in vivo (Abe et al. 1994; Kubo et al. 2003; Reimers et al. 1998). This method is practical for large-scale studies, most notably because of its portability (~10 kg) and ease of taking measurements in the field.

The purpose of the present study was twofold: (1) to investigate the effects of age on cardiorespiratory fitness normalised for regional SM mass, and (2) to determine the relevance of VT normalised to SM mass based on age and gender.

Methods

Subjects

Fourteen hundred and sixty-three healthy Japanese men and women aged 20–80 years participated in this study (807 men and 656 women, 49.3 ± 13.5 years). None of the subjects were taking any medications known to affect the study variables, such as beta-blockers or hormone replacement therapy, and all subjects were members of a fitness club. Most of the subjects routinely performed moderate aerobic and/or resistance exercises. The purpose, procedures and risks were explained to each participant, and all subjects gave their written informed consent before participating in the study approved by the Ethical Commission of Waseda University. Subjects with any of the following conditions were excluded from the study: significant cardiovascular or pulmonary disease, uncontrolled metabolic disease (diabetes, anaemia, or thyroid disease), or electrolyte abnormalities.

Measurement of $\dot{V}O_2peak$ and VT

We measured the body mass, height and waist circumference of all subjects before measurement of $\dot{V}_{O_2peak}$ and VT. $\dot{V}O_2$ during a treadmill walking test was measured using an automated breath-by-breath mass spectrometry system (Aeromonitor AE-280S; Minato Medical Science, Tokyo, Japan). Subjects warmed-up at 40 m min^{-1} on a 4% grade for 3 min. Then, the treadmill speed and grade were increased by 15 m min^{-1} or 5% alternately for each successive minute of walking until subjects reached approximately 85% of their maximum HR (220 minus age). We developed this protocol based on the metabolic equations for gross $\dot{V}O_2$ (American College of Sports Medicine 1990). Previously, we validated this protocol in 104 healthy middle-aged and older men and women (Sanada et al. 1997). Lehmann et al. (1997) confirmed that the treadmill exercise protocol designed on a

theoretical basis to span a range of 0–200 W in increments of approximately 25 W by alteration of either speed or grade from one stage to the next should correspond to a standard bicycle protocol consisting of 25-W steps. $\dot{V}O_2$ during walking was calculated every 30 s. The electrocardiograph was monitored constantly during the exercise session and was also used to measure HR at intervals of 30 s. Ratings of perceived exertion (RPE) were also recorded every minute during exercise. $\dot{V}_{O_2peak}$ was estimated from maximum HR using the HR-$\dot{V}_{O_2}$ relationship for sub-maximal exercise. VT was estimated from ventilatory equivalents for oxygen ($\dot{V}E/\dot{V}_{O_2}$) and carbon dioxide ($\dot{V}E/\dot{V}_{CO_2}$) as described previously (Caiozzo et al. 1982). VT was determined from $\dot{V}_{O_2}$ as the point of inflection where the $\dot{V}E/\dot{V}_{O_2}$ ratio was at its lowest and then increased progressively with further increments in treadmill work rate, while at the same time $\dot{V}E/\dot{V}_{O_2}$ reached a plateau or declined. The modified V-slope method where $\dot{V}_{CO_2}$ was plotted against $\dot{V}_{O_2}$ was also used to support the estimate of VT by ventilatory equivalents (Beaver et al. 1986). In this study, 1,367 (755 men and 612 women) subjects met the criteria for attainment of VT. The VT was similar with a small (< 2%) and not significant difference between the observers. The $\dot{V}_{O_2}$ should be proportional to L^2 or $M^{2/3}$, where L is length and M is body mass (Astrand and Rodahl 1977). We applied this calculation for VT and $\dot{V}_{O_2peak}$.

Ultrasound MTH and measurements

Ultrasound has been widely employed for accurate measurement of the SM size in vivo, and this method has been shown to be highly reliable and valid in previous studies involving measurement of muscle thickness—MTH (Abe et al. 1994; Fukunaga et al. 2001; Reimers et al. 1998). The MTH determined by B-mode ultrasound was assessed at six sites on the anterior and posterior surfaces of the body, as described previously (Abe et al. 1994). The sites included: the anterior and posterior upper arm, a point 60% distal between the lateral epicondyle of the humerus and the acromial process of the scapula; the abdomen, 2–3 cm to the right of the umbilicus; subscapula, 5 cm directly below the inferior angle of the scapula; anterior and posterior thigh surfaces, midway between the lateral condyle of the femur and the greater trochanter.

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, which provided acoustic contact without depression of the skin surface, was placed perpendicular to the tissue interface at the marked sites. The MTHs were measured directly from the screen with electronic callipers, and determined as the distance from the adipose tissue-muscle interface to the muscle–bone interface. Total and regional SM mass were estimated using the equations of Sanada et al. (2005). The 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. Strong correlations were observed between the site-matched SM mass (total, arm, trunk body, thigh and lower leg) for the MRI measurement and MTH × height (in metres) in the model development group (r = 0.83–0.96 in men, r = 0.53–0.91 in women). In addition, the SM mass prediction equations were applied to the validation group, significant correlations were also observed between the MRI-measured and predicted SM mass in vivo(Sanada et al. 2006). Moreover, in another study 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 FFM

FFM was estimated from body density using the subcutaneous fat measurements from B-mode ultrasound, as described previously (Abe et al. 1994). Body density was estimated from measurements at the six subcutaneous fat layer sites, as described in the previous section. The standard error of these estimates using the ultrasound equations was ~0.006 g ml^{-1} (±2.5% body fat) for men and women. Body fat percentage was then calculated from body density using the equation described by Brozek et al. (1963) and FFM was the difference between body mass and fat mass.

Statistical analysis

All measurements and calculated values are expressed as the mean ± standard deviation. One-way ANOVA was used to compare age decade and gender differences for the following physical characteristics: total or regional SM mass and VT or $\dot{V}_{O_2peak}$, body mass, BMI, percent body fat, FFM, waist circumference, total SM mass, trunk SM mass, thigh SM mass and absolute or normalised VT and $\dot{V}_{O_2peak}$ (Tables 1, 2, 3, 4). In cases where a significant F value was obtained, Scheffe's post hoc test was performed to identify significant differences among mean values. Pearson's product correlations were calculated between SM mass and $\dot{V}_{O_2peak}$ or

Table 1 Physical characteristics of subjects

Gender and age range (years)	*n*	Body mass (kg)	Fat-free body mass (kg)	Body mass index (kg m^{-2})	Percent body fat (%)	Waist circumference (cm)
Men						
20–29	55	73.2 ± 10.7†	60.3 ± 5.9†	24.3 ± 3.3	18.2 ± 6.4	73.7 ± 6.7
30–39	110	72.0 ± 9.3†	58.2 ± 6.2†	24.3 ± 2.8	18.8 ± 5.4	75.2 ± 7.8
40–49	205	71.6 ± 9.6†	58.3 ± 6.8†	24.5 ± 3.1	18.2 ± 6.2	77.5 ± 7.2
50–59	205	70.5 ± 9.3†	57.7 ± 6.1†	24.7 ± 2.8	18.0 ± 5.3	80.1 ± 7.8
60–69	167	67.1 ± 7.3	55.3 ± 5.1	24.0 ± 2.2	17.4 ± 3.9	83.3 ± 9.3
70+	65	63.6 ± 5.8	52.9 ± 4.1	23.1 ± 1.7	16.6 ± 3.4	88.1 ± 5.6
All	807	69.9 ± 9.2	57.1 ± 6.2	24.3 ± 2.7	17.9 ± 5.3	87.4 ± 7.7
Women						
20–29	61	53.4 ± 5.8	40.6 ± 3.6	20.6 ± 2.3	23.5 ± 7.1	82.8 ± 9.8†
30–39	158	52.4 ± 7.0	40.1 ± 3.9	20.5 ± 2.5	22.9 ± 6.8	85.7 ± 7.6†
40–49	173	53.3 ± 6.6	40.0 ± 4.1	21.0 ± 2.4	24.2 ± 7.2	87.4 ± 8.3†
50–59	150	53.0 ± 6.7	40.3 ± 3.8	21.4 ± 2.4	23.3 ± 5.8	89.3 ± 7.3
60–69	101	54.0 ± 6.6	40.0 ± 4.4	22.4 ± 2.6	25.8 ± 5.0	87.6 ± 6.6
70+	13	55.4 ± 5.0	41.5 ± 3.5	22.8 ± 2.2	24.9 ± 4.8	86.9 ± 5.9
All	656	53.2 ± 6.6*	40.2 ± 4.0*	21.2 ± 2.5*	23.9 ± 6.4*	78.4 ± 8.4*

† Significant difference in the 70- to 79-year-old group ($P < 0.05$)
*Significant difference in all male subjects ($P < 0.05$)

Table 2 Total and regional SM mass in men and women

Gender and age range (years)	*n*	Total SM mass (kg)	Trunk SM mass (kg)	Thigh SM mass (kg)
Men				
20–29	55	28.1 ± 3.3†	11.6 ± 1.7†	10.5 ± 1.3†
30–39	110	26.5 ± 3.6†	10.8 ± 1.8†	9.9 ± 1.5†
40–49	205	25.7 ± 3.1†	10.4 ± 1.5†	9.6 ± 1.4†
50–59	205	24.8 ± 3.2†	9.9 ± 1.4	9.2 ± 1.4†
60–69	167	23.2 ± 2.5	9.3 ± 1.2	8.6 ± 1.1†
70+	65	21.4 ± 2.1	9.2 ± 1.3	7.8 ± 1.0
All	807	24.8 ± 3.5	10.0 ± 1.6	9.2 ± 1.5
Women				
20–29	61	15.3 ± 2.1	6.3 ± 0.8	5.8 ± 0.8
30–39	158	14.6 ± 2.0	6.0 ± 0.8	5.6 ± 0.8
40–49	173	15.0 ± 2.5	6.1 ± 0.9	5.6 ± 0.9
50–59	150	14.6 ± 2.3	5.9 ± 0.8	5.4 ± 0.8
60–69	101	14.4 ± 2.6	5.9 ± 0.9	5.2 ± 0.9
70+	13	13.9 ± 2.7	5.8 ± 0.7	4.9 ± 1.0
All	656	14.7 ± 2.3*	6.0 ± 0.8*	5.5 ± 0.9*

† Significant difference in the 70- to 79-year-old group ($P < 0.05$)
*Significant difference in all male subjects ($P < 0.05$)

VT (Table 5). Quadratic regression was performed on $\dot{V}_{O_2peak}$ normalised for body mass and linear regression was performed on VT normalised for body mass in men and women (Fig. 1). The alpha level for testing significance was set at $P < 0.05$. All statistical analyses were completed using Stat View v5.0 for windows (SAS Inc., Cary, NC, USA).

Results

The physical characteristics of the male and female subjects are listed in Table 1. Subjects varied in age from 20 to 80 years and body mass index (BMI) from 15.0 to 36.0. The waist circumference increased with age in both genders, but not the % body fat. These results suggest that the accumulation of body fat occurs in abdominal area with age. The reference values for SM mass using the ultrasound method are shown in Table 2. The men had significantly higher SM ($P < 0.001$) in comparison with the women in total, trunk and thigh. Age-associate declines were observed in total, trunk and thigh SM mass in men, but not in women. Tables 3 and 4 show the values for $\dot{V}_{O_2peak}$ and VT in each gender and age group. Age-associated declines were observed for $\dot{V}_{O_2peak}$ normalised for body mass as well as normalised for SM mass (Table 3) in both men and women. Age-associated decline of the absolute VT was observed in men, but not in women. This result is associated with gender differences in SM mass (Table 4). Despite the age-associated declines in VT normalised for body mass in both men and women, VT normalised for SM mass was not significantly different with age.

Table 5 shows simple correlation coefficients among age, and aerobic power in men and women. There were significant negative correlations between age and $\dot{V}_{O_2peak}$ normalised for body mass in men and women, and between age and VT normalised for body mass in men and women. Moreover, there were significant negative correlations between age and SM mass in both men and women.

Significant negative quadratic regression was observed between age and absolute $\dot{V}_{O_2peak}$, while there was a significant negative correlation between age and absolute VT in both men and women (Fig. 1). Signifi-

Table 3 Absolute and normalised $\dot{V}_{O_2peak}$ in various age groups

Gender and age range (years)	*n*	Absolute value (*L*)	Normalised values					
			Body mass (ml kg^{-1} min^{-1})	Body mass$^{2/3}$ (ml kg$^{-2/3}$ min^{-1})	Fat-free body mass (ml kg^{-1} min^{-1})	Total SM mass (ml kg^{-1} min^{-1})	Trunk SM mass (ml kg^{-1} min^{-1})	Thigh SM mas (ml kg^{-1} min^{-1})
Men								
20–29	55	3.44 ± 0.66†	47.2 ± 7.9†	197.1 ± 32.4†	58.7 ± 7.6†	125.9 ± 15.3†	308.5 ± 50.6†	336.4 ± 40.1†
30–39	110	3.15 ± 0.49†	44.3 ± 7.5†	183.3 ± 28.0†	54.1 ± 6.7†	119.8 ± 17.1†	296.8 ± 47.5†	322.2 ± 55.2†
40–49	205	3.04 ± 0.52†	42.6 ± 5.8†	176.3 ± 23.9†	52.3 ± 8.3†	118.7 ± 16.6†	296.7 ± 55.7†	319.9 ± 48.2†
50–59	205	2.71 ± 0.45†	38.7 ± 5.7†	159.7 ± 22.6†	47.2 ± 6.6†	110.6 ± 17.3†	279.2 ± 52.7†	298.6 ± 47.3†
60–69	167	2.39 ± 0.38†	35.7 ± 5.3†	144.8 ± 21.0†	43.2 ± 6.3†	103.7 ± 16.0	260.4 ± 48.2†	280.6 ± 48.0†
70+	65	1.94 ± 0.32	30.7 ± 4.9	122.1 ± 19.5	36.8 ± 5.8	90.9 ± 13.6	214.4 ± 42.4	251.0 ± 41.4
All	807	2.78 ± 0.61	39.8 ± 7.4	163.6 ± 30.9	48.4 ± 9.0	116.6 ± 18.8	315.7 ± 74.2	301.5 ± 53.1
Women								
20–29	61	2.15 ± 0.34†	40.5 ± 6.1†	153.2 ± 22.5†	52.4 ± 8.3†	139.6 ± 22.7†	340.1 ± 65.4†	369.6 ± 66.4†
30–39	158	2.06 ± 0.37†	39.6 ± 6.5†	147.6 ± 23.5†	51.9 ± 7.6†	144.1 ± 24.0†	354.6 ± 75.3†	376.0 ± 60.6†
40–49	173	1.90 ± 0.36	35.9 ± 6.3†	134.3 ± 23.2†	47.6 ± 8.4†	128.5 ± 25.6	317.8 ± 73.1	345.8 ± 66.5
50–59	150	1.76 ± 0.32	33.5 ± 5.7†	125.3 ± 20.8	43.7 ± 6.7†	122.1 ± 21.0	303.5 ± 60.1	332.0 ± 57.5
60–69	101	1.57 ± 0.30	29.1 ± 4.8	109.6 ± 18.0	39.3 ± 6.9	110.8 ± 21.6	270.5 ± 63.6	304.2 ± 63.1
70+	13	1.39 ± 0.26	25.3 ± 50	95.2 ± 18.7	33.6 ± 5.7	101.4 ± 28.0	242.6 ± 60.0	297.2 ± 86.4
All	656	1.87 ± 0.39*	35.4 ± 7.2*	132.5 ± 26.2*	46.5 ± 9.0*	128.2 ± 26.1*	278.2 ± 56.5*	343.8 ± 67.6*

† Significant difference in the 70- to 79-year-old group ($P < 0.05$)

*Significant difference in all male subjects ($P < 0.05$)

cant correlations were observed between the thigh SM mass and absolute $\dot{V}_{O_2peak}$ (Fig. 2) or VT (Fig. 3).

Discussion

To our knowledge, the present study is the first to normalise cardiorespiratory fitness values, including $\dot{V}_{O_2peak}$ and VT, for SM mass using a large population sample. The most notable findings of this study were that absolute $\dot{V}_{O_2peak}$ and VT were closely associated with thigh SM mass independent of age, and the study provided normative cardiorespiratory fitness data based on normalised SM mass in healthy men and women aged 20–80 years. Age-associated declines were also observed in VT normalised for body mass in both men and women; however, VT normalised for SM mass was not significantly different with age. Thus, this cross-sectional study showed that the age-associated declines in VT are markedly blunted if normalised for SM mass rather than body mass. These results suggest that SM mass is closely associated with $\dot{V}_{O_2peak}$ or VT in both men and women, and the decrease in VT with age is primarily due to an age-related decline of SM mass.

In cross-sectional studies, the rates of age-related decline in $\dot{V}_{O_2peak}$ normalised for body mass using treadmill walking or running were in the range of 0.28–0.46 ml kg^{-1} min^{-1} year^{-1} in men and 0.25–0.57 ml kg^{-1} min^{-1} year^{-1} in women (Fleg and Lakatta 1988; Jackson et al. 1995, 1996; Paterson et al. 1999; Talbot et al. 2000; Tanaka and Seals 2003; Toth et al. 1994); values for this study were 0.32 and 0.31 ml kg^{-1} min^{-1} year^{-1} in men and women, respectively (Fig. 1). In addition, previous studies have indicated that the rate of decline in VT is approximately one-third of the rate of decline in $\dot{V}_{O_2peak}$ (Babcock et al. 1992; Cunningham et al. 1985; Posner et al. 1987). Posner et al. (1987) found the rates of decline in VT were 0.08 and 0.07 ml kg^{-1} min^{-1} year^{-1} in men and women, respectively, which are similar to the values from this study (0.09 and 0.10 ml kg^{-1} min^{-1} year^{-1} Fig. 1). However, there is little scientific information about the effect of age on these cardiorespiratory fitness parameters normalised for regional SM mass. A previous study using dual energy X-ray absorptiometry (DXA) to estimate muscle mass showed some variation with a significant decrease in the $\dot{V}_{O_2peak}$ even after normalisation for appendicular muscle mass (Proctor and Joyner 1997). On the other hand, there was no evidence of a decline in VT with age, even when normalised for SM mass. However, in the present study, age-associated declines were also observed for VT normalised for body mass in both men and women. Theoretically, the $\dot{V}_{O_2}$ should be proportional to L^2 or $M^{2/3}$, where L is length and M is body mass. We applied this calculation to VT, and showed that there was an age-related decline in $\dot{V}_{O_2}$ /body mass$^{2/3}$ similarly to $\dot{V}_{O_2}$ /body mass. These results suggest that $\dot{V}_{O_2peak}$ and $\dot{V}_{O_2}$ at VT decrease with age even when taking body dimensions in consideration. This is despite this study showing VT, normalised for SM mass, did not vary

Table 4 Absolute and normalised VT in various age groups

Gender and age range (years)	*n*	Percentage of $\dot{V}_{O_2peak}$ (%)	Absolute value (*L*)	Normalised values					
				Body mass (ml kg^{-1} min^{-1})	Body mass$^{2/3}$ (ml kg$^{-2/3}$ min^{-1})	Fat-free body mass (ml kg^{-1} min^{-1})	Total SM mass (ml kg^{-1} min^{-1})	Trunk SM mass (ml kg^{-1} min^{-1})	Thigh SM mas (ml kg^{-1} min^{-1})
Men									
20–29	47	48.7 ± 7.8†	1.71 ± 0.34†	23.1 ± 4.2†	97.5 ± 16.9†	28.4 ± 4.9†	60.8 ± 9.8	150.2 ± 30.1	162.4 ± 26.7
30–39	98	47.4 ± 8.1†	1.48 ± 0.30†	20.6 ± 3.6†	85.6 ± 15.1†	25.5 ± 4.5†	56.4 ± 10.7	139.5 ± 28.1	151.7 ± 32.2
40–49	195	48.9 ± 7.4†	1.47 ± 0.28†	20.6 ± 3.3†	85.5 ± 13.5†	25.2 ± 4.2†	57.4 ± 8.8	143.8 ± 28.6	154.6 ± 24.4
50–59	185	51.7 ± 8.2†	1.40 ± 0.28†	19.8 ± 3.3	81.6 ± 14.1†	24.2 ± 4.0†	56.6 ± 10.2	142.7 ± 30.1	153.0 ± 28.5
60–69	165	53.3 ± 9 3	1.26 ± 0.22†	18.8 ± 3.2	76.1 ± 12.6	22.8 ± 3.8	54.8 ± 10.5	137.2 ± 30.3	148.2 ± 30.0
70+	65	58.0 ± 10.6	1.11 ± 0.19	17.4 ± 2.3	70.0 ± 9.7	20.9 ± 2.9	51.7 ± 7.5	122.7 ± 25.3	142.8 ± 22.9
All	755	51.1 ± 8.9	1.39 ± 0.31	19.9 ± 3.5	81.9 ± 15.0	24.3 ± 4.4	56.2 ± 9.9	140.1 ± 29.7	151.9 ± 28.1
Women									
20–29	47	51.3 ± 8.0	1.09 ± 0.20	20.5 ± 3.4†	76.9 ± 13.0†	27.2 ± 4.8†	71.6 ± 10.7	174.1 ± 34.8	190.5 ± 30.9
30–39	144	50.4 ± 7.9	1.00 ± 0.22	19.9 ± 3.3†	74.4 ± 12.8†	25.9 ± 4.6†	71.9 ± 13.1	176.9 ± 40.0	187.8 ± 35.2
40–49	161	54.5 ± 7.9	1.03 ± 0.20	19.4 ± 3.5	72.5 ± 13.2	25.7 ± 4.9†	69.4 ± 14.7	171.4 ± 41.2	186.9 ± 39.1
50–59	148	55.4 ± 8.0	0.97 ± 0.18	18.4 ± 3.2	68.5 ± 12.1	24.1 ± 4.1	67.0 ± 12.0	165.8 ± 33.2	182.3 ± 32.9
60–69	100	58.7 ± 9.0	0.90 ± 0.16	16.8 ± 2.5	63.1 ± 9.6	22.7 ± 3.7	63.9 ± 12.3	155.8 ± 34.2	175.3 ± 36.1
70+	12	60.8 ± 9.9	0.86 ± 0.23	15.4 ± 3.2	55.6 ± 10.9	20.6 ± 4.1	58.6 ± 11.2	139.6 ± 31.8	180.8 ± 68.4
All	612	54.3 ± 8.6*	1.00 ± 0.21*	18.8 ± 3.5*	70.5 ± 13.1*	24.9 ± 4.7*	68.5 ± 13.3*	168.4 ± 38.1*	183.9 ± 35.7*

† Significant difference in the 70- to 79-year-old group ($P < 0.05$)

*Significant difference in all male subjects ($P < 0.05$)

with age. These results suggest that the age-related decline of VT, defined by treadmill walking is mainly due mainly to a decline of SM mass.

This could be accounted for by the understanding that $\dot{V}_{O_2peak}$ is limited by central circulatory capacity, while changes in VT reflect peripheral/metabolic alterations with age, such as a loss of mitochondrial content for oxidative phosphorylation (Coggan et al. 1992b). It has been reported that subjects with a higher lactate threshold (LT) have a higher muscle respiratory capacity (Coggan et al. 1992a), and LT is associated with volume density of mitochondria and the surface density of mitochondrial cristae (Drexler et al. 1992) in human SM in vivo. Moreover, in rat SM, LT is determined by peripheral factors, such as mitochondrial oxidative capacity (Hepple et al. 2003). Paterson et al. (1999) suggested that the lower rate of age-associated decline in VT (compared with $\dot{V}_{O_2peak}$) may reflect preserved metabolic function of muscle oxidation and may more closely define endurance capacity, while a greater decline of $\dot{V}_{O_2peak}$ may be due to a loss of oxygen delivery capacity. Since it is well known that slow-twitch fibres have a high mitochondrial density and mitochondrial enzyme activity, these findings suggest that the age-related decline in VT defined by treadmill walking may be associated with an age-related decline of SM mass, reflecting a decrease in active tissue, especially a loss of slow-twitch fibres.

Little information is available on the age-related decline of SM mass (*i.e.*, sarcopenia) using direct measurements, such as MRI or CT, the latter of which is the gold standard. In a cross-sectional study using MRI, Janssen et al. reported an age-related decrease of total body SM mass of 0.18 kg year^{-1} in men and 0.08 kg year^{-1} in women (Janssen et al. 2000); these values were notably higher than those obtained by ultrasound in the present study (0.12 and 0.01 kg year^{-1} in men and women, respectively). Despite these variations, both studies showed the same trend with a greater decrease in total SM mass in men compared to women, and both studies had almost identical differences of ~0.1 kg year^{-1} between men and women. In contrast, a longitudinal study by Song et al. indicated that sarcopenia in total SM mass was 0.37 kg year^{-1} for African American women (Song et al. 2004). In addition to possible ethnic differences, it has been suggested that cross-sectional studies may underestimate actual rates of change in SM mass with age, because these losses may not be linear and could accelerate with age.

The observations of this study are tempered by the limitations inherent to cross-sectional studies. Sta-

Table 5 Simple correlation coefficients among age, body composition, and aerobic power in men and women

	Age (years)	Body mass (kg)	Total SM (kg)	Trunk SM (kg)	Thigh SM (kg)	$\dot{V}_{O_2peak}$ (l min^{-1})
In men						
Body mass (kg)	–0.28					
Total SM (kg)	–0.49	0.76				
Trunk SM (kg)	–0.42	0.55	0.77			
Thigh SM (kg)	–0.47	0.72	0.91	0.55		
$\dot{V}_{O_2peak}$ (l min^{-1})	–0.64	0.55	0.66	0.49	0.63	
VT (l min^{-1})	–0.45	0.57	0.59	0.43	0.58	0.68
In women						
Body mass (kg)	NS					
Total SM (kg)	–0.09	0.68				
Trunk SM (kg)	–0.11	0.42	0.69			
Thigh SM (kg)	–0.20	0.57	0.85	0.37		
$\dot{V}_{O_2peak}$ (l min^{-1})	–0.51	0.34	0.41	0.16	0.48	
VT (l min^{-1})	–0.30	0.44	0.45	0.20	0.47	0.67

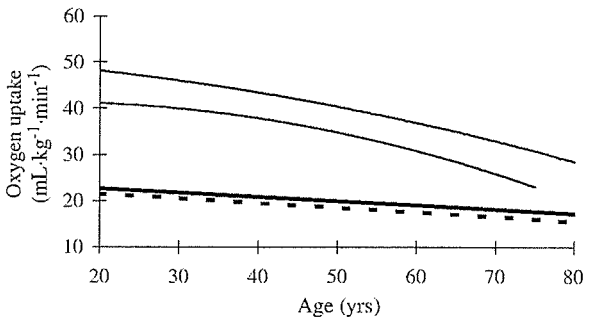

Fig. 1 Relationship between age and cardiorespiratory fitness ($\dot{V}O_2$peak and VT) are shown for men and women. The *thin line* indicates $\dot{V}_{O_2peak}$ and the *heavy line* VT. The *solid line* indicates men and the *dashed line* women. Significant quadratic age declines were observed in $\dot{V}_{O_2peak}$ in men (n = 807, R^2 = 0.34, Y = 50.989–0.096x–0.002x^2, P < 0.001) and women (n = 656, R^2 = 0.32, Y = 40.605–0.122x–0.005x^2, P < 0.001). On the other hand, VT declined linearly with age in men (n = 755, R^2 = 0.12, Y = 24.549–0.091x, P < 0.001) and women (n = 612, R^2 = 0.13, Y = 23.623–0.102x, P < 0.001)

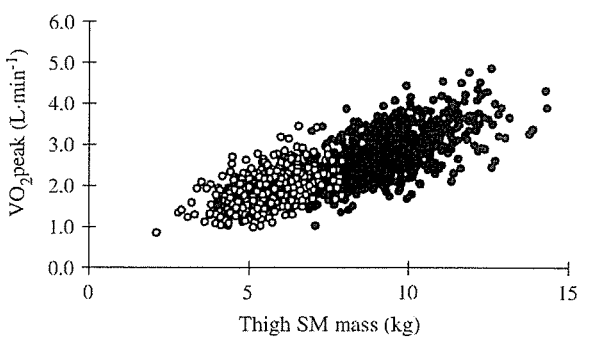

Fig. 2 Relationship between thigh SM mass and $\dot{V}_{O_2peak}$ values in men (*closed circles*) and women (*open circles*). Significant correlations were observed between the thigh SM mass and $\dot{V}_{O_2peak}$. Men; n = 755, y = 0.265x + 0.332, r = 0.63, P < 0.001. Women; n = 620, y = 0.215x + 0.681, r = 0.48, P < 0.001

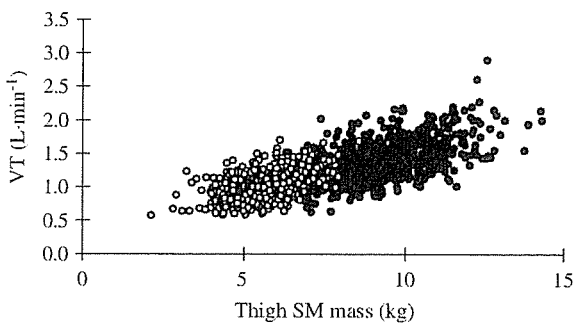

Fig. 3 Relationship between thigh SM mass and VT values in men (closed circles) and women (open circles). Significant correlations were observed between the thigh SM mass and VT. Men; n = 755, y = 0.119x + 0.297, r = 0.58, P < 0.001. Women; n = 612, y = 0.112x + 0.382, r = 0.47, P < 0.001

thokostas et al. (2004) investigated longitudinal data versus cross-sectional analysis, and showed a greater decline in VT for men (0.14 ml kg^{-1} min^{-1} year^{-1}) and women (0.11 ml kg^{-1} min^{-1} year^{-1}). Second, this study assessed the total or regional SM mass by ultrasound. MTH measurements using ultrasound may not be accurate as compared to MRI, and the measurement of SM size by B-mode ultrasound has limitations because it cannot exclude non-contractive tissue, such as the connective and intra-muscular fat tissue. Third, $\dot{V}_{O_2peak}$ was estimated at sub-maximal effort, which may introduce substantial error. However, this study had a large sample size including many middle-aged and older men and women, and there is a certain degree of risk with graded exercise tests (GXT) in subjects with low fitness levels or in the elderly (American College of Sports Medicine 1995). We configured the end point of the GXT to prevent such risks. In addition, Wasserman et al. (1995) noted that in calculating using the V-slope method, the data

above the $\dot{V}_{O_2}$ at which $VE/\dot{V}_{CO_2}$ starts to increase (respiratory compensation point) should not be included. Since we calculated the VT by this method, VT could be estimated at sub-maximal GXT. Moreover, the $\dot{V}_{O_2}$ values at VT in the present study correspond to those reported in previous studies (Posner et al. 1987; Thomas et al. 1985). Finally, the treadmill protocol in this study which alternates the speed and grade has the potential to give a non-linear increase in estimated work rate, because it uses rather large steps to increase the grade. However, we ensured a linear increase in $\dot{V}_{O_2}$ during this protocol in the majority of subjects. Therefore, we might as well to evaluate the ventilatory threshold using our protocol.

In conclusion, we have demonstrated that absolute $\dot{V}_{O_2peak}$ and VT were closely associated with thigh SM mass independent of age, body mass and FFM. Age-associated declines were observed in VT normalised for body mass in both men and women, but not VT normalised for SM mass. These results suggest that thigh SM mass was closely associated with $\dot{V}_{O_2peak}$ or VT in both men and women, and the decrease in VT with age is due, in part, to an age-related decline of SM mass. Moreover, this study provides normative cardiorespiratory fitness data regarding VT normalised SM mass in healthy men and women aged 20–80 years.

References

Abe T, Kondo M, Kawakami Y, Fukunaga T (1994) Prediction equations for body composition of Japanese adults by B-mode ultrasound. Am J Hum Biol 6:161–170

American College of Sports Medicine (1995) Guidelines for exercise testing and prescription, Lippincott Williams & Wilkins, Philadelphia

American College of Sports Medicine (1990) American College of Sports Medicine position stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults. Med Sci Sports Exerc 22:265–274

Astrand PO, Rodahl K (1977) Textbook of work physiology. Physiological bases of exercise, McGraw-Hill, NY

Babcock MA, Paterson DH, Cunningham DA (1992) Influence of ageing on aerobic parameters determined from a ramp test. Eur J Appl Physiol Occup Physiol 65:138–143

Beaver WL, Wasserman K, Whipp BJ (1986) A new method for detecting anaerobic threshold by gas exchange. J Appl Physiol 60:2020–2027

Blair SN, Kohl HW III, Paffenbarger RS, Jr, Clark DG, Cooper KH, Gibbons LW (1989) Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA 262:2395–2401

Blair SN, Kohl HW III, Barlow CE, Paffenbarger RS, Jr, Gibbons LW, Macera CA (1995) Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. JAMA 273:1093–1098

Brozek J, Grande F, Anderson JT, Keys A (1963) Densitometric analysis of body composition: revision of some quantitative assumptions. Ann NY Acad Sci 110:113–140

Caiozzo VJ, Davis JA, Ellis JF, Azus JL, Vandagriff R, Prietto CA, McMaster WC (1982) A comparison of gas exchange indices used to detect the anaerobic threshold. J Appl Physiol 53:1184–1189

Coggan AR, Kohrt WM, Spina RJ, Kirwan JP, Bier DM, Holloszy JO (1992a) Plasma glucose kinetics during exercise in subjects with high and low lactate thresholds. J Appl Physiol 73:1873–1880

Coggan AR, Spina RJ, King DS, Rogers MA, Brown M, Nemeth PM, Holloszy JO (1992b) Histochemical and enzymatic comparison of the gastrocnemius muscle of young and elderly men and women. J Gerontol 47:B71–B76

Cunningham DA, Nancekievill EA, Paterson DH, Donner AP, Rechnitzer PA (1985) Ventilation threshold and aging. J Gerontol 40:703–707

Drexler H, Riede U, Munzel T, Konig H, Funke E, Just H (1992) Alterations of skeletal muscle in chronic heart failure. Circulation 85:1751–1759

Fleg JL, Lakatta EG (1988) Role of muscle loss in the age-associated reduction in V_{O_2max}. J Appl Physiol 65:1147–1151

Fletcher GF, Balady G, Blair SN, Blumenthal J, Caspersen C, Chaitman B, Epstein S, Sivarajan Froelicher ES, Froelicher VF, Pina IL, Pollock ML (1996) Statement on exercise: benefits and recommendations for physical activity programs for all Americans. A statement for health professionals by the Committee on Exercise and Cardiac Rehabilitation of the Council on Clinical Cardiology, American Heart Association. Circulation 94:857–862

Frontera WR, Suh D, Krivickas LS, Hughes VA, Goldstein R, Roubenoff R (2000) Skeletal muscle fiber quality in older men and women. Am J Physiol Cell Physiol 279:C611–C618

Fukunaga T, Miyatani M, Tachi M, Kouzaki M, Kawakami Y, Kanehisa H (2001) Muscle volume is a major determinant of joint torque in humans. Acta Physiol Scand 172:249–255

Gaskill SE, Ruby BC, Walker AJ, Sanchez OA, Serfass RC, Leon AS (2001) Validity and reliability of combining three methods to determine ventilatory threshold. Med Sci Sports Exerc 33:1841–1848

Hepple RT, Hagen JL, Krause DJ, Jackson CC (2003) Aerobic power declines with aging in rat skeletal muscles perfused at matched convective O_2 delivery. J Appl Physiol 94:744–751

Jackson AS, Beard EF, Wier LT, Ross RM, Stuteville JE, Blair SN (1995) Changes in aerobic power of men, ages 25–70 years. Med Sci Sports Exerc 27:113–120

Jackson AS, Wier LT, Ayers GW, Beard EF, Stuteville JE, Blair SN (1996) Changes in aerobic power of women, ages 20–64 years. Med Sci Sports Exerc 28:884–891

Janssen I, Heymsfield SB, Wang ZM, Ross R (2000) Skeletal muscle mass and distribution in 468 men and women aged 18–88 years. J Appl Physiol 89:81–88

Kawakami Y, Abe T, Fukunaga T (1993) Muscle-fiber pennation angles are greater in hypertrophied than in normal muscles. J Appl Physiol 74:2740–2744

Kubo K, Kanehisa H, Azuma K, Ishizu M, Kuno SY, Okada M, Fukunaga T (2003) Muscle architectural characteristics in women aged 20–79 years. Med Sci Sports Exerc 35:39–44

Lehmann G, Schmid S, Ammer R, Schomig A, Alt E (1997) Evaluation of a new treadmill exercise protocol. Chest 112:98–106

McArdle W, Katch FI, Katch VL (2001) Exercise physiology: energy, nutrition, and human performance. Lippincott Williams & Wilkins, Philadelphia

Paterson DH, Cunningham DA, Koval JJ, St Croix CM (1999) Aerobic fitness in a population of independently living men and women aged 55–86 years. Med Sci Sports Exerc 31:1813–1820

Posner JD, Gorman KM, Klein HS, Cline CJ (1987) Ventilatory threshold: measurement and variation with age. J Appl Physiol 63:1519–1525

Proctor DN, Joyner MJ (1997) Skeletal muscle mass and the reduction of V_{O_2max} in trained older subjects. J Appl Physiol 82:1411–1415

Reimers CD, Harder, T, Saxe H (1998) Age-related muscle atrophy does not affect all muscles and can partly be compensated by physical activity: an ultrasound study. J Neurol Sci 159:60–66

Sanada K, Kuchiki T, Takao Y, Horii M, Kyuunou, S, Hatori Y (1997) References of exercise prescription in ideal old aged that considered to individual differences in fitness levels (in Japanese). Ono Sports Sci 5:71–86

Sanada K, Kearns CF, Kojima K, Abe T (2005) Peak oxygen uptake during running and arm cranking normalized to total and regional skeletal muscle mass measured by magnetic resonance imaging. Eur J Appl Physiol 93:687–693

Sanada K, Kearns CF, Midorikawa, Abe T (2006) Prediction and validation of total and regional skeletal muscle mass by ultrasound in Japanese adults. Eur J Appl Physiol 96:24–31

Song MY, Ruts E, Kim J, Janumala I, Heymsfield S, Gallagher D (2004) Sarcopenia and increased adipose tissue infiltration of muscle in elderly African American women. Am J Clin Nutr 79:874–880

Stathokostas L, Jacob-Johnson S, Petrella RJ, Paterson DH (2004) Longitudinal changes in aerobic power in older men and women. J Appl Physiol 97:781–789

Talbot LA, Metter EJ, Fleg JL (2000) Leisure-time physical activities and their relationship to cardiorespiratory fitness in healthy men and women 18–95 years old. Med Sci Sports Exerc 32:417–425

Tanaka H, Seals DR (2003) Invited review: dynamic exercise performance in Masters athletes: insight into the effects of primary human aging on physiological functional capacity. J Appl Physiol 95:2152–2162

Thomas SG, Cunningham DA, Thompson J, Rechnitzer PA (1985) Exercise training and "ventilation threshold" in elderly. J Appl Physiol 59:1472–1476

Toth MJ, Gardner AW, Ades PA, Poehlman ET (1994) Contribution of body composition and physical activity to age-related decline in peak V_{O_2} in men and women. J Appl Physiol 77:647–652

Tuomainen P, Peuhkurinen K, Kettunen R, Rauramaa R (2005) Regular physical exercise, heart rate variability and turbulence in a 6-year randomized controlled trial in middle-aged men: the DNASCO study. Life Sci 77:2723–2734

Wasserman K, Hansen JE, Sue DY, Stringer WW, Whipp BJ (2005) Principles of exercise testing and interpretation: including pathophysiology and clinical applications. Lippincott Williams & Wilkins, Philadelphia

Zhang JG, Ohta T, Ishikawa-Takata K, Tabata I, Miyashita M (2003) Effects of daily activity recorded by pedometer on peak oxygen consumption (V_{O_2peak}), ventilatory threshold and leg extension power in 30- to 69-year-old Japanese without exercise habit. Eur J Appl Physiol 90:109–113

Resistance training and arterial compliance: keeping the benefits while minimizing the stiffening

Hiroshi Kawano[a,b,c], Hirofumi Tanaka[d] and Motohiko Miyachi[a]

Objectives This study aimed to determine the effects of moderate resistance training as well as the combined resistance and aerobic training intervention on carotid arterial compliance.

Background Resistance training has become a popular mode of exercise, but intense weight training is shown to stiffen carotid arteries.

Methods Thirty-nine young healthy men were assigned either to the moderate-intensity resistance training (MODE), the combined resistance training and endurance training (COMBO) or the sedentary control (CONTROL) groups. Participants in the training groups underwent three training sessions per week for 4 months followed by four additional months of detraining.

Results All training groups increased maximal strength in all the muscle groups tested ($P < 0.05$). Carotid arterial compliance (via simultaneous carotid ultrasound and applanation tonometry) decreased approximately 20% after MODE training (from 0.20 ± 0.01 to 0.16 ± 0.01 mm^2/mmHg, $P < 0.01$). No significant changes in carotid arterial compliance were observed in the COMBO (0.20 ± 0.01 to 0.23 ± 0.01 mm^2/mmHg) and CONTROL (0.20 ± 0.01 to 0.20 ± 0.01 mm^2/mmHg) groups. Following the detraining period, carotid arterial compliance returned to the baseline level. Peripheral (femoral) artery compliance did not change in any groups.

Conclusions We concluded that simultaneously performed aerobic exercise training could prevent the stiffening of carotid arteries caused by resistance training in young healthy men. *J Hypertens* 24:1753–1759 © 2006 Lippincott Williams & Wilkins.

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Introduction

The aorta and large arteries play an important role in the cardiovascular system not only as blood conduits to the peripheral tissues, but also as a buffer for pressure changes resulting from intermittent ventricular ejection of blood. By absorbing a proportion of the energy in systole and releasing it in diastole, they maintain coronary blood flow and avoid an increase in left ventricular afterload. Through the impairment of this buffering function, reductions in arterial compliance or increases in arterial stiffness contribute to elevations in systolic blood pressure, left ventricular hypertrophy, and coronary ischemia [1,2]. Indeed, higher arterial stiffness is associated with a greater rate of mortality in patients with end-stage renal failure and essential hypertension [3,4]. Accordingly, any interventions that could act to decrease arterial compliance should be cautiously performed or even avoided.

Resistance training has become a popular modality of exercise performed by most populations, and has become an integral component of exercise recommendations endorsed by a number of national health organizations [5–7]. Resistance training has profound effects on the musculoskeletal system, thereby contributing to the maintenance of functional capacity and the prevention of sarcopenia and osteoporosis [7]. The effects of resistance training on the cardiovascular system, however, are not well understood. We have recently demonstrated that high-intensity resistance training is associated with reduced arterial compliance [8,9]. This finding was initially observed in cross-sectional studies comparing strength-trained individuals and sedentary controls [8] and later confirmed by interventional studies involving several months of resistance training interventions [9]. Considering a number of functional and physiological benefits that resistance training induces, practice of resistance training should not be discouraged. A remaining critical question is whether any type of resistance training could be performed regularly without inducing arterial stiffening. In this context, two strategies appear plausible. First, the intensity and volume of the resistance training used in the previous studies [8,9] were more strenuous and vigorous than those recommended for the comprehensive health programs [5–7]. It is not currently

known whether moderate resistance training would induce similar arterial stiffening. Second, because regular aerobic exercise has been shown to increase arterial compliance [10,11], simultaneously performed endurance training may negate the effects of resistance training, thereby attenuating or preventing arterial stiffening. Neither of these possibilities has been tested, however.

Accordingly, the primary aim of the present study was to determine the effects of moderate-intensity resistance training as well as the combined strength and endurance training intervention on carotid arterial compliance. We hypothesized that the compliance of carotid arteries would not change following moderate-intensity resistance training as well as combined resistance and aerobic training. At the completion of the exercise intervention period, we implemented a period of detraining. We reasoned that if the observed changes in arterial compliance were induced by the prescribed exercise training, values should return to the baseline levels when the stimuli of exercise training were removed.

Methods

Participants

A total of 39 young healthy men were studied. None of the men had participated in any resistance or endurance training on the regular basis. All subjects were normotensive (< 140/90 mm Hg), non-obese (body mass index < 30 kg/m^2), and free of overt chronic diseases as assessed by medical history, physical examination, and a complete blood chemistry and hematological evaluation. Candidates who smoked in the past 4 years were taking cardiovascular-acting medications or anabolic steroids, or had significant intima–media thickening, plaque formation, and/or other characteristics of atherosclerosis (e.g. ankle–brachial index < 0.9) were excluded. All subjects gave their written informed consent to participate, and all procedures were reviewed and approved by the Institutional Review Board. Subjects were randomly assigned into either the moderate-intensity resistance training group (MODE, $n = 12$), the combined high-intensity resistance training and moderate-intensity aerobic exercise training group (COMBO, $n = 11$), or sedentary control group (CONTROL, $n = 16$). No endurance-training group was included because the primary focus of the present study was on resistance training. Before the intervention period, there were no significant differences in any of the variables between the groups (Table 1).

Table 1 Selected subject characteristics at baseline

Variable	CONTROL group	MODE group	COMBO group
N	16	12	11
Age (years)	22 ± 1	20 ± 1	21 ± 1
Height (cm)	172 ± 1	169 ± 2	171 ± 2
Body weight (kg)	68 ± 2	65 ± 2	66 ± 2
Body mass index (kg/m^2)	22 ± 1	23 ± 1	23 ± 1
Body fat (%)	21 ± 1	18 ± 2	21 ± 1
Lean body mass (kg)	55 ± 2	51 ± 1	53 ± 1
Peak oxygen consumption (ml/kg per min)	49 ± 3	52 ± 2	49 ± 2

Data presented as the mean ± SEM. CONTROL, sedentary control group; MODE, moderate-intensity resistance training group; COMBO, combined high-intensity resistance training and moderate-intensity aerobic exercise training group.

Measurements

The exercise intervention groups were studied five times: before training (baseline), at 2 months (midpoint of exercise training), at 4 months (completion of exercise training), at 6 months (midpoint of detraining), and at 8 months (completion of detraining). The non-exercising control group was studied three times: baseline, at 4 months, and at 8 months. In order to avoid potential diurnal variations, subjects were tested at the same time of day throughout the study period [9,10]. Furthermore, prior to each testing, subjects abstained from caffeine and fasted for at least 4 h; most subjects were studied after overnight fast. Subjects in the intervention groups were studied 20–24 h after their last exercise training session to avoid the acute effects of exercise [12], but while they were still considered to be in their normal (i.e. habitually exercising) physiological state.

incremental exercise

To demonstrate that the participants had been sedentary, we measured the maximal oxygen consumption during an incremental cycle ergometer exercise [13]. The oxygen consumption, heart rate, and ratings of perceived exertion were measured throughout the protocol.

Strength testing

Maximal muscular strength in the intervention groups was assessed before and after resistance training using the following exercises: half squat, bench press, leg extension, leg curls, lat row, and abdominal bend. After 10 warm-up repetitions, one-repetition maximum (1 RM) values were obtained according to established guidelines. The day-to-day coefficient of variation for 1 RM strength in our laboratory is 4 ± 2%. The 1 RM test was not performed in the control group due to the potential risks involved in the testing.

Body composition

The body composition was determined using the bioelectric impedance method (coefficient of variance, 4 ± 2%) [14].

Arterial blood pressure at rest

Chronic levels of arterial blood pressure at rest were measured with a semi-automated oscillometric device (Form PWV/ABI; Colin Medical, Komaki, Aichi, Japan) over the brachial and dorsalis pedis artery. Recordings were made in triplicate with participants in the supine position.

Carotid artery intima–media thickness

The carotid artery intima–media thickness (IMT) was measured from the images derived from an ultrasound machine equipped with a high-resolution linear-array broad-band transducer as previously described [8]. Ultrasound images were analyzed by use of computerized image analysis software. At least 10 measurements of IMT were taken at each segment, and the mean values were used for analysis. This technique has excellent day-to-day reproducibility (coefficient of variance, $3 \pm 1\%$) for the carotid IMT.

Carotid artery stiffness and compliance

A combination of ultrasound imaging of the pulsatile common carotid artery with simultaneous applanation of tonometrically obtained arterial pressure from the contralateral carotid artery permits non-invasive determination of arterial compliance [10,15]. The carotid artery diameter was measured from images derived from an ultrasound machine equipped with a high-resolution linear-array transducer. A longitudinal image of the cephalic portion of the common carotid artery was acquired 1–2 cm distal to the carotid bulb. To assess the effects of peripheral artery compliance, the same procedure was repeated on the common femoral artery. All image analyses were performed by the same investigator who was blinded to the group assignments.

Pressure waveforms and amplitudes were obtained from the common carotid artery with a pencil-type probe incorporating a high-fidelity strain-gauge transducer (SPT-301; Millar Instruments, Houston, Texas, USA) [10,16]. Because baseline levels of blood pressure are subjected to hold-down force, the pressure signal obtained by tonometry was calibrated by equating the carotid mean arterial and diastolic blood pressure to the brachial artery value [9,10]. In addition to arterial compliance [17], we also calculated the β-stiffness index, which provides an index of arterial compliance adjusted for distending pressure [18]. Arterial compliance and the β-stiffness index were calculated using the equations $[(D_1-D_0)/D_0]/[2(P_1-P_0)] \times \pi \times (D_0)^2$ and $[\ln(P_1/P_0)]/[(D_1-D_0)/D_0]$, where D_1 and D_0 are the maximal and minimum diameters, and P_1 and P_0 are the highest and lowest blood pressures. The blood pressure obtained at the ankle (Form PWV/ABI; Colin Medical) was used to calculate the femoral artery compliance. The day-to-day coefficients of variation were 2 ± 1, 7 ± 3, and 5 ± 2 for the carotid artery diameter, pulse pressure, and arterial compliance, respectively. The coefficient of variance for femoral arterial compliance was $7 \pm 4\%$.

Left ventricular dimensions, mass and function

Echocardiography was used to measure the left ventricular dimensions, wall thickness, and stroke volume according to established guidelines [19] as previously described [8]. The left ventricular mass and stroke volume were normalized for the body surface area. The ratio of the average left ventricular wall thickness to the left ventricular internal end-diastolic diameter was used as an index of relative wall thickness [8].

Exercise training intervention

In the first 4 months of study period, participants in all training groups underwent three supervised resistance training sessions per week. During each training session, participants in the COMBO group completed three sets of 8–12 exercises at 80% of 1 RM and subjects in the MODE group completed three sets of 14–16 exercises at 50% of 1 RM, in the following order: leg extension, seated chest press, leg curls, lateral row, squat, and sit-ups. The resistance of each exercise was increased progressively throughout the resistance training period. The recovery time between exercise bouts was controlled at 2-min intervals. Each resistance training session lasted approximately 45 min. Subjects in the COMBO group performed a cycle exercise at 60% of the maximal heart rate for 30 min immediately after each resistance training session. Training assistants verbally encouraged the subjects and ensured proper form and technique at each exercise session. Participants were instructed to refrain from any other regular exercise during the entire study period. Participants in the sedentary control group were instructed not to alter their normal activity levels throughout the study period.

Statistical analyses

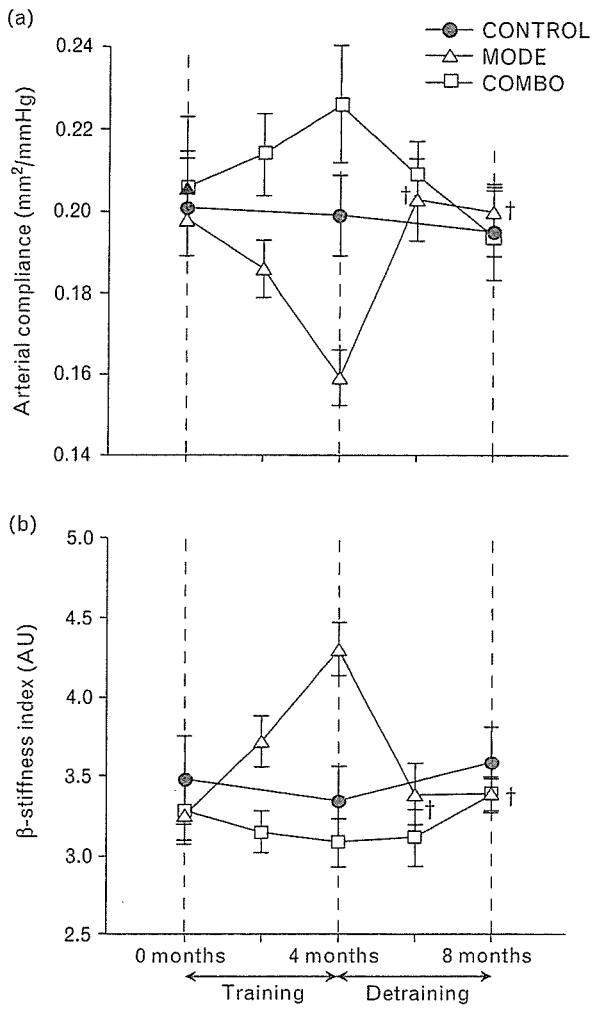
Changes were assessed by two-way analysis of variance (group × time) with repeated measures. In the case of significant F-values, a post-hoc test (Newman–Keuls method) was used to identify significant differences among mean values. To determine whether the changes in arterial compliance and the β-stiffness index were independent of changes in stroke volume, analysis of covariance was performed with stroke volume as the covariate. Pearson's correlation and regression analyses were performed to determine the relation between variables of interest.

Results

Before the intervention period, there were no significant differences in any of the variables between the groups (Table 1). In all groups, there were no changes in height, weight, body mass index, and body surface area throughout the intervention periods.

All the exercise intervention groups increased 1 RM strength significantly in all muscle groups tested ($P < 0.05$ to $P < 0.0001$). Percentage increases in 1 RM strength for the MODE and COMBO groups were 6 and 25% for leg extension, 13 and 14% for leg curl, 10 and 25% for squat, 8 and 17% for lateral row, 6 and 21% for bench press, and 12 and 21% for abdominal bend, respectively.

Fig. 1



Changes in (a) carotid arterial compliance and (b) β-stiffness index for the sedentary control group (CONTROL), the moderate-intensity strength training group (MODE), and the combined aerobic and strength training group (COMBO). Data presented as the mean ± SEM. *$P < 0.05$ versus baseline; †$P < 0.05$ versus 4 months.

Table 2 Hemodynamic and vascular indices

Variable	Baseline	After training	After detraining	Interaction
Brachial systolic blood pressure (mmHg)				
CONTROL group	118 ± 2	119 ± 1	120 ± 2	$F = 2.130$
MODE group	120 ± 3	117 ± 3	115 ± 2	$P = 0.086$
COMBO group	115 ± 2	116 ± 2	115 ± 2	
Brachial diastolic blood pressure (mmHg)				
CONTROL group	68 ± 2	73 ± 2*	73 ± 1	$F = 5.475$
MODE group	71 ± 2	66 ± 2*	68 ± 2	$P > 0.001$
COMBO group	67 ± 1	67 ± 2	67 ± 2	
Brachial pulse pressure (mmHg)				
CONTROL group	49 ± 2	47 ± 1	47 ± 1	$F = 2.407$
MODE group	49 ± 2	52 ± 2	47 ± 2	$P = 0.057$
COMBO group	48 ± 2	49 ± 1	48 ± 1	
Carotid systolic blood pressure (mmHg)				
CONTROL group	101 ± 2	104 ± 2	104 ± 1	$F = 1.653$
MODE group	105 ± 3	105 ± 4	104 ± 3	$P = 0.170$
COMBO group	99 ± 2	97 ± 2	98 ± 2	
Carotid pulse pressure (mmHg)				
CONTROL group	33 ± 2	32 ± 1	32 ± 1	$F = 2.383$
MODE group	36 ± 2	39 ± 3	36 ± 2†	$P = 0.059$
COMBO group	31 ± 1	30 ± 1	32 ± 1	
Carotid lumen diameter (mm)				
CONTROL group	5.91 ± 0.11	5.94 ± 0.14	6.06 ± 0.11	$F = 1.839$
MODE group	6.03 ± 0.13	6.02 ± 0.10	6.02 ± 0.11	$P = 0.131$
COMBO group	5.79 ± 0.09	5.91 ± 0.07	5.81 ± 0.09	
Δ Carotid lumen diameter (mm)				
CONTROL group	0.66 ± 0.03	0.66 ± 0.04	0.63 ± 0.03	$F = 3.460$
MODE group	0.74 ± 0.02	0.66 ± 0.04*	0.76 ± 0.04†	$P = 0.012$
COMBO group	0.71 ± 0.04	0.72 ± 0.03	0.69 ± 0.04	
Carotid intima–media thickness (mm)				
CONTROL group	0.50 ± 0.01	0.52 ± 0.02	0.50 ± 0.02	$F = 1.803$
MODE group	0.46 ± 0.01	0.45 ± 0.02	0.46 ± 0.01	$P = 0.138$
COMBO group	0.47 ± 0.01	0.52 ± 0.01	0.51 ± 0.02	
Femoral compliance (mm²/mmHg)				
CONTROL group	0.10 ± 0.01	0.09 ± 0.01	0.08 ± 0.01	$F = 0.950$
MODE group	0.08 ± 0.01	0.09 ± 0.01	0.08 ± 0.01	$P = 0.441$
COMBO group	0.09 ± 0.01	0.07 ± 0.01	0.07 ± 0.01	

Data presented as the mean ± SEM. CONTROL, sedentary control group; MODE, moderate-intensity resistance training group; COMBO, combined high-intensity resistance training and moderate-intensity aerobic exercise training group. *$P < 0.05$ versus baseline. †$P < 0.05$ versus after the training period.

The magnitude of increases was larger ($P < 0.05$) in the COMBO group than in the MODE group in all exercises except for the leg curl.

There were no significant differences in baseline arterial compliance and β-stiffness index between all four groups (Fig. 1). Carotid arterial compliance decreased after 4 months of MODE interventions ($P < 0.01$). In contrast, arterial compliance did not decrease, but rather tended to increase ($P = 0.06$), after 4 months of the COMBO intervention. Following the detraining period, arterial compliance values returned to the baseline level. Alterations in arterial compliance were primarily due to changes in arterial distension as the carotid pulse pressure remained unchanged (Table 2). In general, qualitatively similar results (although inverse in direction) were obtained by use of the β-stiffness index ($P < 0.01$). The femoral arterial compliance, an index of the compliance of peripheral (muscular) artery, did not change in any groups. In all groups, there were no significant changes in brachial and carotid systolic blood pressures, carotid IMT, and carotid lumen diameter (Table 2).

In all groups, there were no significant changes in heart rate at rest throughout the study period (Table 3). All the resistance training interventions increased the left ventricular mass index and the relative wall thickness ($P < 0.001$). In the COMBO group, the stroke volume index tended to increase during the training period ($P = 0.07$). There were no significant changes in the stroke volume index in any other groups. Following the detraining period, left ventricular structural and functional indices returned to baseline and were no longer significantly different from baseline. There were no such changes in the sedentary control group throughout the study period. To determine whether changes in stroke volume, a determinant of arterial compliance, could confound the interpretation of the present results, we performed several different analyses. When we performed a

Table 3 Cardiac indices

Variable	Baseline	4 months	8 months	Interaction
Heart rate at rest (beats/min)				
CONTROL group	58 ± 3	56 ± 2	57 ± 2	$F = 0.254$
MODE group	55 ± 3	54 ± 2	53 ± 2	$P = 0.906$
COMBO group	52 ± 3	48 ± 1	50 ± 1	
Left ventricular mass index (g/m^2)				
CONTROL group	131 ± 7	132 ± 7	131 ± 7	$F = 11.940$
MODE group	139 ± 4	151 ± 4*	137 ± 4†	$P < 0.001$
COMBO group	125 ± 5	143 ± 6*	127 ± 6†	
Relative wall thickness (%)				
CONTROL group	19.5 ± 0.4	19.7 ± 0.4	19.8 ± 0.4	$F = 15.793$
MODE group	19.0 ± 0.5	20.7 ± 0.5*	19.3 ± 0.5†	$P < 0.001$
COMBO group	19.0 ± 1.0	20.2 ± 0.9*	18.9 ± 0.9†	
Stroke volume index (ml/m^2)				
CONTROL group	47 ± 2	47 ± 2	46 ± 2	$F = 1.861$
MODE group	51 ± 1	50 ± 1	50 ± 1	$P = 0.130$
COMBO group	48 ± 2	50 ± 2	48 ± 2	

Data presented as the mean ± SEM. CONTROL, sedentary control group; MODE, moderate-intensity resistance training group; COMBO, combined high-intensity resistance training and moderate-intensity aerobic exercise training group. *$P < 0.05$ versus baseline. †$P < 0.05$ versus 4 months.

univariate correlation analysis between the stroke volume index and carotid arterial compliance in a pooled population, these two functions were not correlated ($r = 0.05$, $P = 0.93$). Additionally, changes in carotid arterial compliance were not associated with changes in stroke volume index in the combined exercise group ($r = 0.19$, $P = 0.26$). Moreover, when analysis of covariance was performed with the stroke volume as the covariate, the overall results on carotid arterial compliance were essentially the same.

Discussion

The major findings of the present study are as follows. First, resistance training performed at a moderate intensity produced a magnitude of arterial stiffening similar to high-intensity resistance training previously reported [9]. Second, concurrently performed endurance training minimized arterial stiffening that was accompanied by high-intensity resistance training. These results suggest that a simultaneously performed aerobic training could negate and prevent the stiffening of carotid arteries caused by resistance training.

Historically, resistance training had been regarded as unsafe for individuals at high risk for future cardiac events because of the abrupt increases in blood pressure and myocardial oxygen demand during high-intensity resistance training [20]. These marked increases in arterial blood pressure during resistance exercise were thought to be initiating factors for arterial stiffening [8]. The majority of recent studies, however, have documented that low to moderate resistance training is a safe and viable form of exercise training as blood pressure increases are within the clinically acceptable range during moderate-intensity resistance training [21]. For these reasons, we hypothesized that resistance training performed at a moderate intensity would not result in a decrease in arterial compliance. In contrast to our working hypothesis, moderate resistance training significantly decreased arterial compliance (from 0.20 ± 0.01 to 0.16 ± 0.01 $mm^2/mmHg$), and the magnitude of the reduction in arterial compliance was similar to that we previously observed in high-intensity resistance training (from 0.20 ± 0.02 to 0.16 ± 0.01 $mm^2/mmHg$) [9]. Moreover, these changes in arterial compliance returned to the baseline levels a few months after the cessation of training, confirming that the change in carotid arterial compliance was indeed due to the effect of the moderate resistance training intervention. Furthermore, reductions in arterial compliance were accompanied by significant increases in left ventricular mass index and relative wall thickness, important clinical correlates of arterial stiffening. Even moderate-intensity resistance training therefore appears to stiffen or harden the large elastic arteries. Our present study provides a warning that even moderate resistance training, which is typically recommended to the general public, should be prescribed cautiously, especially for high-risk populations. However, one important consideration that should be emphasized is that the volume (i.e. three sets) of moderate-intensity resistance training used in the present study was still greater than that typically recommended for comprehensive health programs, where only one set of resistance exercises is recommended [6,7]. We therefore cannot exclude the possibility that moderate-intensity resistance training performed with fewer sets may not result in a reduction in arterial compliance.

In contrast to resistance training, regular aerobic exercise is shown to be efficacious in preventing and reversing arterial stiffening in healthy adults [10,11]. We hypothesized that by combining the stiffening effects of resistance training and the destiffening effects of endurance training, both interventions would negate each other and would cause no changes in arterial compliance. In the present study, we demonstrated that simultaneously performed endurance training prevented the reduction in arterial compliance that was accompanied by high-intensity resistance training. Additionally, there was a tendency for arterial compliance to increase with combined endurance and resistance training. From the standpoint of exercise adherence and compliance, this type of 'cross-training' is highly beneficial as it is more enjoyable and breaks the boredom that often results from long-term participation in a single exercise mode [22,23]. Taken together, these findings suggest that combined resistance and aerobic training may be an effective countermeasure for the unfavorable effects of strenuous resistance training.

It is not clear what physiological mechanisms explain the effects of combined training on arterial compliance. Chronic or repeated increases in flow exert their effects on endothelial vasodilatation by modulating the expression of nitric oxide synthase [24]. Carotid arteries