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【原　著】

「健康づくりのための運動基準 2006」における「健康づくりのための最大酸素摂取量」の基準値と生命予後の関係：日本人男性労働者を対象にしたコホート研究

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【要約】目的：厚生労働省は「健康づくりのための運動基準 2006」の中で「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を示している。しかしながら，この値や範囲と生命予後の関係について疫学的な検討を行った研究は見当たらない。そこで，本研究はこれらの値や範囲と生命予後の関係を明らかにすることを目的に，コホート研究のデータを解析した。

方法：本研究の対象者は日本人男性労働者 8,935 人であり，年齢の中央値および四分位範囲は 35（29～43）歳であった。1982 年から 1988 年の間に実施した自転車エルゴメータを用いた最大下運動負荷テストの結果から最大酸素摂取量を推定した。対象者を「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を用いて各年代別に「範囲以下」群（Ⅰ群），「範囲の下限から基準値以下」群（Ⅱ群），「基準値から範囲の上限以下」群（Ⅲ群），「範囲の上限超」群（Ⅳ群）の 4 群に分類した後，2003 年 6 月 30 日までの死亡情報を確認した。各群別に死亡の相対危険度を算出するために比例ハザードモデルを用いた。そして，年齢，BMI，収縮期血圧，飲酒習慣，喫煙習慣を調整した多変量調整ハザード比および 95%信頼区間を求めた。

結果：観察期間中に 360 人が死亡した。Ⅰ群を基準にした場合のⅡ群，Ⅲ群，Ⅳ群の多変量調整ハザード比および 95%信頼区間は 0.76（0.58-0.99），0.59（0.43-0.80），0.80（0.49-1.31）であった（トレンド検定：p=0.009）。

結論：日本人男性労働者において「健康づくりのための最大酸素摂取量」の基準値を上回る最大酸素摂取量を持つ群は総死亡リスクが低いことが示された。

Key words：運動負荷テスト，最大酸素摂取量，疫学研究，相対危険度，運動基準

1．緒　言

2006 年，厚生労働省は 1989 年に発表した「健康づくりのための運動所要量」を 17 年ぶりに改定し，「健康づくりのための運動基準 2006～身体活動・運動・体力～」を発表した[1)]。この基準では，体力と生活習慣病あるいは生命予後との関係について調査した論文をシステマティックレビューして，「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を示している。システマティックレビューに採用された研究の多くは欧米人を対象に実施された研究であり，それらの論文から得られた基準値および範囲が日本人の生活習慣病罹患や生命予後とどのような関係にあるか，日本人を対象に評価を行うことが重要であり，これまでにいくつかの報告がなされている[2-4)]。しかしながら，この値や範囲と生命予後の関係について日本人を対象に疫学的な検討を行った研究は見当たらない。また，「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を国内に普及させるにあたって，日本人を対象に本基準や範囲と生命予後の関係を明

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らかにしておくことは重要であると考えられる。そこで，本研究は日本人を対象に「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と生命予後の関係を明らかにすることを目的にコホート研究のデータを解析した。

2．研究方法

2-1．対象者

本研究は，首都圏に都市ガスを供給する会社である東京ガス株式会社の社員を対象に実施された。対象者は，1982 年 3 月末時点において東京ガス株式会社に在席していた 12,899 人（男性：11,978 人，女性：921 人）から選定された。女性は人数が少ないことから本研究の対象から除いた。また，1982 年から 1988 年の間に実施した健康診断において循環器系疾患，がん，糖尿病，消化器系疾患あるいは結核と判定された対象者を除いた（1,162 人）。更に，運動負荷テストに先立って実施した問診において内科的もしくは整形外科的疾患があると答えた対象者を除いた（1,777 人）。加えて，「健康づくりのための最大酸素摂取量」の年代別基準値は 20 歳未満の基準値が示されていないことから 20 歳未満の社員（104 人）を対象から除いた。最終的に本研究の対象者は，8,935 人の男性労働者（年齢：20～59 歳）となった。

本研究は労働安全衛生法に基づくとともに，疫学研究に関する倫理指針（文部科学省，厚生労働省）を遵守して実施された。

2-2．定期健康診断

対象者は労働安全衛生法に基づき定期健康診断を受診した。健康診断結果から身長，体重，安静時血圧値を解析に用いた。身長，体重の測定から，Body Mass Index（BMI：体重[kg]/身長[m]^2）を求め，体格の指数とした。安静時血圧は，椅子座位で 3 分間以上の安静の後，水銀血圧計によって計測した。血圧値が高い場合には複数回計測して低い値を採用した。また，自己記入式質問票を用いて飲酒習慣および喫煙習慣を確認した。

2-3．運動負荷テスト

最大下運動負荷テストを実施して最大酸素摂取量を推定した。運動負荷は，モナーク社製自転車エルゴメータを用いて各段階 4 分間の最大下負荷を最大で 3 段階かけた。1 段階目の負荷は年齢別に 19～29 歳，30～39 歳，40～49 歳，50～59 歳それぞれ 600 kilopond meter (kpm)，525 kpm，450 kpm，375 kpm であった。2 段階目以降は年齢に関係なく 225 kpm 増加させた。年齢から推定した最大心拍数（220－年齢）の 85%を目標心拍数に設定し，目標心拍数に到達した者はその時点で運動負荷テストを中止した。最終段階の最後の 1 分間から得られた仕事量と最後の 10 秒間から得られた心拍数から Åstrand と Ryhming のノモグラム [5] と Åstrand の年齢補正係数 [6] を用いて最大酸素摂取量を推定した。

2-4．ベースライン調査および追跡調査

対象者が 1982 年から 1988 年の間で定期健康診断と最大下運動負荷テストを最初に同じ年に受けた際のデータを，追跡開始前の値（ベースラインデータ）として採用した。そして，2003 年 6 月 30 日までの死亡情報を確認した。在職者の死亡については，人事情報をもとに，医療スタッフが死亡者の所属する職場総務担当者に対する電話聞き取り調査によって死因を確認した。退職後の死亡については，退職者で組織された会の事務局による家族に対する電話聞き取り調査によって死因を確認した。退職時に退職者で組織された会に入会しなかった 311 人（3.4%）については，死亡の記録を把握できないことから，退職時点で観察打ち切りとした。追跡期間中の全死亡者について，死因を ICD-10（International Statistical Classification of Diseases and Related Health Problems, Tenth Revision）の死因分類表に従って分類した。

2-5．解析方法

対象者を，「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（表 1）を用いて，各年代別に「範囲以下」群（I 群），「範囲の下限から基準

表 1　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（男性）

	20 歳代	30 歳代	40 歳代	50 歳代	60 歳代
基準値	40	38	37	34	33
範　囲	33 - 47	31 - 45	30 - 45	26 - 45	25 - 41

値以下」群(II群),「基準値から範囲の上限以下」群(III群),「範囲の上限超」群(IV群)の4群に分類した。分類した群間の身体的特徴については,連続数は一元配置分散分析,飲酒率および喫煙率についてはKruskal-Wallis testを用いて群間の差を検討した。

各群別に死亡の相対危険度を算出するために比例ハザードモデルを用いた。そして,年齢調整ハザード比および95%信頼区間を求めた。更に年齢以外の交絡因子として,BMI(連続数),収縮期血圧(連続数),飲酒習慣(非飲酒・アルコール45g/日以下・46g/日以上),喫煙習慣(非喫煙もしくは禁煙,20本/日未満,20本/日以上)のベースラインデータを調整した多変量調整ハザード比および95%信頼区間を求めた。また,最大酸素摂取量と生命予後の間に量反応関係があるかどうかについてトレンド検定を行った。

統計解析には,SPSS 15.0J for Windows (SPSS, Chicago, IL)を使用した。有意水準はp値を0.05として,p値がこれより小さければ統計的に有意と判定した。

3. 結　果

年代別にみた追跡開始時点における対象者の身体的特徴を表2に示した。年齢の中央値は35歳であった。最大酸素摂取量や喫煙率は年代が高いほど低い値を示していた。一方,拡張期血圧については年代が高いほど高い値を示していた。飲酒率については年代が高いほど高い値を示しているが,50歳代は20歳代と同じような値を示していた。また,BMIや収縮期血圧については年代との明確な関係は認められなかった。これらの対象者を約20年追跡した結果,360人が死亡した。死因の内訳はがん(ICD : 2000-2202)が185人,循環器疾患(ICD : 9000-9500)が91人,その他(79人),不明(5人)であり,死因の51%をがん死亡が占めていた。

表3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を基に分類した群別にみた対象者の身体的特徴を示した。II群とIII群に60%以上が含まれ,I群は18.0%,IV群は9.7%であった。I群からIV群に向けてBMI,収縮期血圧,拡張期血圧が低い値を示していた。飲酒率や喫煙率につ

表2　年代別にみた追跡開始時点における対象者の身体的特徴

	人数 (人)	年齢 a) (歳)	BMI b) (kg/m²)	最大酸素摂取量 b) (ml/kg/分)	収縮期血圧 b) (mmHg)	拡張期血圧 b) (mmHg)	飲酒率 (%)	喫煙率 (%)
全年代	8,935	35 (29-43)	22.7 ± 2.5	36.9 ± 6.8	124.3 ± 12.1	73.6 ± 10.7	72.9	63.6
20-29歳	2,663	27 (25-28)	22.3 ± 2.5	40.4 ± 6.8	125.2 ± 11.4	69.6 ± 11.0	69.8	71.2
30-39歳	3,035	34 (32-36)	22.8 ± 2.5	36.8 ± 6.4	124.0 ± 12.2	73.0 ± 10.4	74.6	64.4
40-49歳	2,295	43 (41-46)	22.9 ± 2.4	34.4 ± 6.0	123.2 ± 12.3	76.8 ± 9.6	75.1	55.6
50-59歳	942	53 (51-55)	22.7 ± 2.7	33.2 ± 5.8	125.7 ± 13.1	78.7 ± 9.1	70.8	58.7

a) 中央値(四分位範囲)　b) 平均値±標準偏差

表3　「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を基に分類した群別にみた対象者の身体的特徴

	人数 (人)	年齢 (歳)	BMI (kg/m²)	最大酸素摂取量 (ml/kg/分)	収縮期血圧 (mmHg)	拡張期血圧 (mmHg)	飲酒率 (%)	喫煙率 (%)
I群 a)	1,611	37.7 ± 7.9	24.2 ± 2.6	28.4 ± 2.8	127.3 ± 12.1	77.0 ± 9.9	72.7	62.2
II群 b)	3,753	36.9 ± 9.3	23.0 ± 2.4	34.5 ± 2.8	124.8 ± 11.9	74.4 ± 10.5	74.1	64.3
III群 c)	2,702	36.0 ± 9.3	21.8 ± 2.2	40.9 ± 2.7	122.8 ± 12.3	72.0 ± 10.6	71.5	63.8
IV群 d)	869	31.4 ± 7.9	21.3 ± 2.0	50.4 ± 4.5	121.4 ± 11.6	68.7 ± 11.0	72.5	62.5
p値 e)	—	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.002	0.027

a) I群:範囲以下　b) II群:範囲の下限から基準値以下　c) III群:基準値から範囲の上限以下　d) IV群:範囲の上限超
e) 一元配置分散分析もしくはKruskal-Wallis test

いては一定の傾向を示さなかった。

「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を基に分類した群別にみた総死亡の年齢調整および多変量調整ハザード比を表4に示した。Ⅰ群を基準にした場合のⅡ群，Ⅲ群，Ⅳ群の多変量調整ハザード比および95%信頼区間は0.76 (0.58-0.99)，0.59(0.43-0.80)，0.80(0.49-1.31)であり，各群と総死亡の間に統計的に有意な負の量反応関係が認められた（p = 0.009）。Ⅰ群と比較して，「健康づくりのための最大酸素摂取量」範囲内であるⅡ群およびⅢ群はいずれも統計的に有意に低いハザード比を示した。また，範囲内であっても最大酸素摂取量がより高いⅢ群はⅡ群と比較して統計的に有意に低いハザード比（0.73[0.56-0.96]）を示した。一方，Ⅳ群については明確な関係を示さなかった。

死因をがんおよび循環器疾患に限定して各群と死亡の関係を調査した結果を，表5に示した。「健

表4　「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を基に分類した群別にみた総死亡のハザード比

	人数	追跡人年	死亡者数	10,000人年当たりの死亡者数	年齢調整ハザード比	95%信頼区間	多変量調整ハザード比[e]	95%信頼区間
Ⅰ群[a]	1,611	32,238	84	26	1.00	—	1.00	—
Ⅱ群[b]	3,753	75,814	164	22	0.78	0.60 - 1.01	0.76	0.58 - 0.99
Ⅲ群[c]	2,702	54,756	90	16	0.63	0.47 - 0.85	0.59	0.43 - 0.80
Ⅳ群[d]	869	17,595	22	12	0.84	0.53 - 1.35	0.80	0.49 - 1.31
					p = 0.017[f]		p = 0.009[f]	

a) Ⅰ群:範囲以下　b) Ⅱ群:範囲の下限から基準値以下　c) Ⅲ群:基準値から範囲の上限以下　d) Ⅳ群:範囲の上限超
e) 調整項目:年齢, BMI, 収縮期血圧, 飲酒習慣, 喫煙習慣
f) トレンド検定

表5　「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を基に分類した群別にみたがんおよび循環器死亡のハザード比

	人数	追跡人年	死亡者数	10,000人年当たりの死亡者数	年齢調整ハザード比	95%信頼区間	多変量調整ハザード比[e]	95%信頼区間
がん死亡								
Ⅰ群[a]	1,611	32,238	39	12	1.00	—	1.00	—
Ⅱ群[b]	3,753	75,814	92	12	0.92	0.63 - 1.34	0.87	0.59 - 1.28
Ⅲ群[c]	2,702	54,756	43	8	0.64	0.41 - 0.98	0.57	0.36 - 0.90
Ⅳ群[d]	869	17,595	11	6	0.93	0.48 - 1.83	0.85	0.42 - 1.70
					p = 0.094[f]		p = 0.046[f]	
循環器死亡								
Ⅰ群[a]	1,611	32,238	26	8	1.00	—	1.00	—
Ⅱ群[b]	3,753	75,814	37	5	0.55	0.33 - 0.90	0.58	0.35 - 0.97
Ⅲ群[c]	2,702	54,756	24	4	0.52	0.30 - 0.91	0.55	0.31 - 1.00
Ⅳ群[d]	869	17,595	4	2	0.52	0.18 - 1.51	0.57	0.20 - 1.74
					p = 0.040[f]		p = 0.082[f]	

a) Ⅰ群:範囲以下　b) Ⅱ群:範囲の下限から基準値以下　c) Ⅲ群:基準値から範囲の上限以下　d) Ⅳ群:範囲の上限超
e) 調整項目:年齢, BMI, 収縮期血圧, 飲酒習慣, 喫煙習慣
f) トレンド検定

康づくりのための最大酸素摂取量」の基準値および範囲を基に分類した各群とがん死亡の関係について評価したトレンド検定は，統計的に有意な負の関係を示したが，個々の群別にみると，Ⅲ群のみⅠ群より有意に低いハザード比を示していた。一方，循環器疾患による死亡については，年齢調整ハザード比に関するトレンド検定の結果は統計的に有意な負の関係を示していたが（トレンド検定：p = 0.040），年齢以外の交絡因子を調整すると両者の関係が弱くなった（トレンド検定：p = 0.082）。多変量調整ハザード比について個々の群別にみると，Ⅰ群と比較してⅡ群のみ統計的に有意に低いハザード比を示していた。

ベースライン調査時に顕在化していなかった潜在的疾患が原因で低い最大酸素摂取量を示した人たちが存在し，因果の逆転バイアスをもたらす可能性がある。そこで追跡開始6年以降の打ち切りデータのみを利用した解析を行ったが（対象：8,854人），全データを用いた解析と同様の結果であり，Ⅰ群を基準にした場合のⅡ群，Ⅲ群，Ⅳ群における総死亡の多変量調整ハザード比および95%信頼区間は0.75(0.57-0.99)，0.59(0.43-0.82)，0.73(0.43-1.22)であった(トレンド検定:p = 0.006)。

4．考　察

本研究は，厚生労働省が2006年に発表した「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と生命予後の関係について日本人男性労働者を対象に疫学的に調査した。20年間の追跡期間中，360人が死亡した。「基準値の範囲以下群(Ⅰ群)」と比較して，「健康づくりのための最大酸素摂取量」範囲内である「範囲の下限から基準値以下の群(Ⅱ群)」および「基準値から範囲の上限以下の群(Ⅲ群)」はいずれも統計的に有意に低いハザード比を示した。また，範囲内であっても最大酸素摂取量がより高いⅢ群はⅡ群と比較して低いハザード比を示した。一方，「基準値の範囲を超える群(Ⅳ群)」については明確な関係を示さなかった。

4-1．最大酸素摂取量と総死亡

Kodamaらは，最大酸素摂取量と総死亡の関係について33本の論文をシステマティックレビューして，最大酸素摂取量の1 MET（3.5 ml/kg/minute）の低下が総死亡のリスクを13%上昇させると報告している[7]。本研究においても，「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を基に分類した各群と総死亡は，統計的に有意な負の量反応関係が認められた(p = 0.009)。一方，Ⅳ群についてはハザード比がⅡ群やⅢ群より高い値を示していた。本研究におけるⅣ群は「健康づくりのための最大酸素摂取量」の基準値の範囲の上限を超える群であり，他の群と比較して人数が少ないことによる統計的な不安定さによりハザード比が逆転した可能性が考えられた。

4-2．がん死亡および循環器系疾患による死亡

本研究は「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が日本人の生命予後とどのような関係にあるかについて評価を行うことを目的に実施していることから，日本人における死因の上位を占めるがん死亡および循環器系疾患による死亡についてサブ解析を実施した。

これまでに実施された最大酸素摂取量とがん死亡の関係を調査したコホート研究は，両者の間に負の量反応関係があることを報告している[8-11]。本研究ではⅠ群と比較してⅢ群は有意に低いハザード比を示していることから，「健康づくりのための最大酸素摂取量」の基準値以上の値を維持することによってがん死亡が抑制される可能性があると考えられる。

最大酸素摂取量と循環器系疾患による死亡の関係を調査したコホート研究については，欧米人を対象に実施された研究において両者の間に負の量反応関係があることが報告されている[7,8,12]。本研究においては両者の間に統計的に有意な関係が認められなかったが，これはがん死亡と比較して循環器系疾患による死亡者数が少なく，統計的な検出力が低いことが原因である可能性が考えられた。また，明確な量反応関係は認められなかったがⅠ群と比較してⅡ群は統計的に有意に低いハザード比を示しており，循環器系疾患による早世予防のために「健康づくりのための最大酸素摂取量」の範囲以上の値を維持することが重要であると考えられる。

4-3．本研究の特徴

コホート研究によって「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と生命予後の関係を評価している点が本研究の特徴である。また，本研究は日本人を対象にしており，欧米人を

対象に実施されたコホート研究を多く含むシステマティックレビューの結果から作成された基準値および範囲について日本人を対象に評価している点も本研究の特徴となっている。

4-4. 本研究の課題

本研究にはいくつかの課題が存在する。第1に，本研究における最大酸素摂取量は間接法を使用して推定した値であり，実測値ではなく推定誤差を含んだ値となっている。しかしながら Teräslinna らは，欧米人を対象に実施された研究ではあるが我々が用いた方法と同じ推定方法と実測した値を比較した結果，相関係数が 0.92 であったと報告しており[13]，本研究で用いた推定値はある程度信頼のおける値であると考えられる。第2に対象者に関する課題がある。本研究は，「女性を対象としていない」，「60 歳以上を対象としていない」，「健康な労働者のみを対象にしている」といった課題があることに加え，東京周辺に居住している特定企業の労働者のみを対象としていることから日本人男性労働者としての代表性に課題があると考えられる。今後，本研究とは異なる対象者をコホートとした研究が報告されることが望まれる。第3として，死因の把握方法が課題となる。本研究では死因を電話による聞き取り調査によって把握しており，死亡診断書や死亡小票を確認する方法と比較して死因の把握が不正確であると考えられる。

5．結　論

日本人男性労働者において「健康づくりのための最大酸素摂取量」の基準値を上回る最大酸素摂取量をもつ群は総死亡リスクが低いことが示された。

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【Original Article】

Reference Values of the Maximal Oxygen Uptake on "Exercise and Physical Activity Reference for Health Promotion 2006" and Mortality: A Cohort Study among Japanese Male Workers

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Abstract

Purpose: In 2006, the Ministry of Health, Labour and Welfare published "Exercise and Physical Activity Reference for Health Promotion 2006". This report showed reference values and ranges of the maximal oxygen uptake for health promotion. However, there are no epidemiological studies that have investigated the relationship between these values and ranges in relation to mortality. Therefore, we assessed the existing data of our cohort study among Japanese male workers.

Methods: Subjects were 8,935 Japanese male workers. The median age was 35 years old (IQR: 29 to 43). The maximum oxygen uptake was estimated using a submaximal cycle ergometer test between 1982 and 1988. The men were classified into four groups based on the reference values and ranges, the below the range group (Group I), the bottom of the range to below the reference value group (Group II), the reference value to the upper range group (Group III), and the over the range group (Group IV). We investigated mortality until June 30, 2003. We used the proportional hazards model in order to obtain the relative risks (RR) for mortality across each group. Multivariate RR and 95% confidence intervals (95% CI) for mortality were obtained while adjusting for age, systolic blood pressure, cigarette smoking, and alcohol intake.

Results: There were 360 deaths during the follow-up period. Using Group I as reference, the RR and 95% CI for Group II to Group IV were 0.76 (0.58-0.99), 0.59 (0.43-0.80), and 0.80 (0.49-1.31), respectively (p for trend = 0.009).

Conclusion: These findings suggest that Japanese male workers in the upper range of the reference values of maximal oxygen uptake for health promotion have a lower RR of mortality.

Key words: exercise test, maximal oxygen uptake, epidemiology, relative risk, Exercise and Physical Activity Reference for Health Promotion 2006

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Mitochondrial Macrohaplogroup Associated with Muscle Power in Healthy Adults

Authors

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Key words
- mtDNA
- polymorphism
- haplogroup
- physical fitness
- leg extension power
- vertical jump

Abstract

The present study was undertaken to examine the effect of mitochondrial haplogroups on aerobic and anaerobic performance phenotypes such as maximum oxygen consumption, muscle power, and muscle mass. We recruited 474 healthy Japanese individuals and measured their physical performance phenotypes such as peak oxygen uptake, muscle power, and muscle mass. The genotypes for 186 polymorphisms in the mitochondrial DNA were determined, and the haplotypes were classified into 2 macrohaplogroups (i.e., N and M) and 12 haplogroups (i.e., F, B, A, N9a, N9b, M7a, M7b, G1, G2, D4a, D4b, and D5). When we compared the 2 major Japanese macrohaplogroups, leg extension power ($P=0.0395$), leg extension power based on body weight ($P=0.0343$), and vertical jump performance ($P=0.0485$) were significantly higher in subjects with mitochondrial macrohaplogroup N than in those with macrohaplogroup M. However, peak oxygen uptake was similar between the 2 groups. When we analyzed the 12 haplogroups, all of the measured parameters were similar among them. In conclusion, mitochondrial macrohaplogroup N may be one of the determinant factors of anaerobic physical performance phenotype such as muscle power.

Introduction

It is commonly believed that genetic factors are major determinants of physical performance phenotypes such as maximal oxygen uptake [4,12] and muscle strength [3,27]. Recently, over 200 genes, in both the nuclear and mitochondrial genomes, have been suggested to have an effect on physical performance and health-related fitness [5]. Mitochondria are essential to all higher organisms for sustaining life, and are extremely important in energy metabolism, providing 36 molecules of ATP per glucose molecule in contrast to the 2 ATP molecules produced by glycolysis. Although most DNA is packaged in chromosomes within the nucleus, mitochondria also possess their own circular DNA, i.e., mitochondrial DNA (mtDNA). The 16569-bp human mtDNA contains 13 genes for the mitochondrial oxidative phosphorylation (OXPHOS) system, as well as 2 rRNA and 22 tRNA genes that are necessary for protein synthesis within mitochondria [2].

It is believed that certain mtDNA polymorphisms and/or mitochondrial haplogroups, which are defined by the presence of a characteristic cluster of tightly linked mitochondrial DNA polymorphisms, are related to aerobic performance and its phenotypes. Indeed, a number of studies reported that mitochondrial haplogroups are positively or negatively associated with elite endurance athlete status [7,24,30] and maximal oxygen uptake [23] and trainability [9,26]. We previously reported that elite Kenyan and Japanese endurance athletes differed in their mitochondrial haplogroup distribution relative to the general Kenyan and Japanese populations, respectively [24,30]. Although numerous studies have reported associations between aerobic performance phenotypes and mitochondrial haplogroups, studies on associations between anaerobic performance phenotypes and mitochondrial haplogroups are lacking. Because anaerobic capacity relies more heavily upon glycolysis than upon mitochondrial OXPHOS, it is not commonly believed that certain mtDNA polymorphisms and/or mitochondrial haplogroups are related to anaerobic capacity. However, we found significant associations between mitochondrial haplogroup F and elite sprint/power athlete status as well as between mitochondrial haplogroup G1 and elite endurance/middle-power athlete status in Japanese Olympi-

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ans [24]. More recently, we reported significant associations between mitochondrial haplogroups and sprint/power athlete status in African-Americans [8].

Although the molecular mechanisms remain largely unknown, we can hypothesize that certain mtDNA polymorphisms and/or mitochondrial haplogroups are not only associated with aerobic performance but also associated with anaerobic performance phenotypes. Furthermore, patients with mutations in mtDNA commonly present with exercise intolerance, muscle weakness, and increased production of lactate [29]. Therefore, the present study was undertaken to examine the effect of mitochondrial haplogroups on aerobic and anaerobic performance phenotypes such as peak oxygen uptake (VO_2peak), muscle power, and muscle mass.

Methods

Subjects

A total of 474 adults comprising 140 men and 334 women, 23–79 years of age, participated in the present study. Written consent was obtained from each subject, and the study was approved by the Ethics Committees of the National Institute of Health and Nutrition and Tokyo Metropolitan Institute of Gerontology. The study was performed in accordance with the guidelines of the Declaration of Helsinki. This study was also performed according to ethical standard in sports and exercise science research of the International Journal of Sports Medicine [18].

Anthropometry and biochemical analysis

Body weight and height were measured to the nearest 0.1 cm and 0.1 kg, respectively, and body mass index (BMI: kg/m^2) was calculated by dividing the body weight (kg) by the square of height (m^2). Total body fat (fat mass, FM) and %fat were obtained from dual-energy x-ray absorptiometry (DXA or DEXA; Hologic QDR-4500A scanner, Hologic, Waltham, MA, USA). Blood pressure was measured with a Form (Omron Colin, JAPAN) under a quiet resting condition in the supine position.

Venous blood samples were drawn from the subjects in the seated position and were obtained after overnight fasting for at least 12 h. Whole blood hemoglobin A1c (HbA1c) concentration was determined by use of an enzymatic method (Mitsubishi Chemical Medicine, Tokyo, Japan). Blood samples were prepared as plasma or serum and stored at −20 °C until the time of analysis. Plasma glucose concentration, serum total cholesterol, HDL (high density lipoprotein)-cholesterol, triglyceride, and insulin concentrations were also determined enzymatically (Mitsubishi Chemical Medicine).

Measurements of peak oxygen uptake (VO_2peak)

VO_2peak was measured by an incremental cycle exercise test using a cycle ergometer (828E; Monark, Varberg, Sweden) [25]. The incremental cycle exercise began at a work rate of 90 W (60–120 W) in men and 60 W (30–90 W) in women, and power output was increased by 15 W/min until the subjects could not maintain a fixed pedalling frequency of 60 rpm. The subjects were encouraged during the ergometer test to exercise at the level of maximum intensity. Heart rate and rating of perceived exertion (RPE) were monitored per minute during exercise. RPE was obtained with the modified Borg scale. VO_2 was monitored during the last 30 s of each increase in work rate. Subjects breathed through a low-resistance 2-way valve, and the expired air was collected in Douglas bags. Expired O_2 and CO_2 gas concentrations were measured by mass spectrometry (ARCO-1000A; Arco System, Chiba, Japan), and expired gas volume was determined with a dry gas meter (DC-5C; Shinagawa Seiki, Tokyo, Japan). VO_2peak was assessed by the attainment of 3 of the following 4 criteria: 1) a plateau in VO_2 with increases in external work, 2) maximal respiratory exchange ratio ≥ 1.1, 3) maximal heart rate of the age-predicted maximum [208 − 0.7 * age (year)] ≥ 90 % [31], and 4) RPE ≥ 18; the highest value of VO_2 during the exercise test was then designated as VO_2peak.

Measurements of muscle power, muscle strength, and muscle mass

Three indicators of muscle power or strength were measured: leg extension power, vertical jump, and isometric hand grip strength. The leg extension power was measured by using a dynamometer (Anaero Press 3500; Combi Wellness, Tokyo, Japan) in the sitting position. The subjects were advised to vigorously extend their legs. 5 trials were performed at 15-s intervals, and the average of the 2 highest recorded power outputs (watt; W) was taken as the definitive measurement [36]. Vertical jump was measured by use of a jump meter (JUMP-MD T.K.K. 5406; TAKEI, Tokyo, Japan). The subjects were given 2 attempts to jump as high as possible from the floor, after having been allowed only to bend their knees before jumping. The height they jumped (centimeters, cm) was measured by determining the length of a line fixed at one end to a belt around a subject's waist and attached by its other end to a platform on the ground. Hand grip strength was measured using a Grip Strength dynamometer (GRIP-D T.K.K 5401; TAKEI, Tokyo, Japan). The dynamometer was adjusted individually for hand size, and 2 trials were performed for each hand. For the present study, the maximum strength obtained for either the right or left hand was used as the measure of hand grip strength (kg).

Total fat-free mass (FFM) were assessed by DXA using the previously described method [28]. Briefly, subjects were positioned for whole-body scans according to the manufacturer's protocol. Participants lay in the supine position on the DXA table with their limbs close to their bodies. The whole body FFM was divided into several regions, i.e., arms, legs, trunk and head, to estimate appendicular FFM (sum of arms and legs), leg FFM, and arm FFM. The body compositions were analyzed 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. For minimization of inter-observer variation, all scans and analyses were carried out by well disciplined investigators, and the day-to-day CV of their observations was 2.95 % for FFM in the whole body.

Physical activity levels

Physical activity was evaluated using of a triaxial accelerometer (Actimarker EW4800; Panasonic Electric Works, Osaka, Japan). The subjects were asked to wear a waist belt for 20 days except during water activities. The metabolic equivalent (MET) intensity levels of physical activity were calculated as described previously [16]. The average step count (steps/day) and average METs·h were calculated using data obtained for at least 14 days,

Table 1 Background characteristics of the subjects separated into mitochondrial macrohaplogroups N and M.

	Macrohaplogroup		
	N (n=151)	M (n=323)	*P* value
age (year)	51±1.0	53±0.7	0.0932
sex (male/female)	47/104	93/230	0.6657
height (cm)	161.4±0.7	160.0±0.5	0.1027
weight (kg)	60.0±0.9	59.3±0.7	0.5087
BMI (kg/m^2)	23.0±0.3	23.0±0.2	0.8985
ratio of waist/hip	0.89±0.005	0.90±0.004	0.1455
SBP (mm Hg)	120±1	121±1	0.8860
DBP (mm Hg)	71±1	72±1	0.3846
glucose (mg/dL)	93±1	94±1	0.6885
HbA1c (%)	5.1±0.04	5.1±0.03	0.6018
IRI (μU/mL)	4.8±0.3	4.6±0.2	0.5557
TG (mg/dL)	98±6	93±3	0.4647
total-cholesterol (mg/dL)	207±3	212±2	0.1871
HDL-cholesterol (mg/dL)	63±1	64±1	0.5516

Data are means±SEM. SBP: systolic blood pressure, DBP: diastolic blood pressure, IRI: immunoreactive insulin, TG: triglyceride, HDL: high-density lipoprotein

Table 2 Physical characteristics of the subjects separated into mitochondrial macrohaplogroups N and M.

	Macrohaplogroup		
	N (n=151)	M (n=323)	*P* value
leg extension power (kW)	**1.12±0.04**	**1.03±0.03**	**0.0395**
leg extension power (W/kg BW)	**18.3±0.5**	**17.1±0.3**	**0.0343**
hand grip strength (kg)	32.8±0.7	32.1±0.5	0.3898
vertical jump (cm)	**38.0±0.9**	**36.0±0.6**	**0.0485**
step count (steps/day)	10985±290	11176±199	0.5863
physical activity (Mets/h)	3.86±0.20	4.01±0.12	0.4813
$\dot{V}O_2$peak (mL·kg^{-1}·min^{-1})	30.9±0.6	30.2±0.4	0.3312
heart rate max (bpm)	174±±1	173±1	0.2870
fat mass (kg)	16.1±0.4	16.2±0.3	0.9357
%fat	26.4±0.6	26.9±0.4	0.5163
FFM (kg)	44.8±±0.7	44.0±0.5	0.3850
appendicular FFM (kg)	19.1±0.4	18.7±0.3	0.3388
RSMI	7.25±0.09	7.20±0.07	0.6808

Data are means±SEM. Bold type indicates significant differences between macrohaplogroups N and M. W: watts, $\dot{V}O_2$peak: peak oxygen uptake, FFM: fat-free mass, RSMI: relative skeletal muscle index

and days when the belt was not worn or the step count was under 1 000 steps/day were excluded.

Haplogroup analysis

Total DNA was isolated from venous blood by use of a QIAamp DNA Blood Maxi Kit (QIAGEN, Hilden, Germany). The entire mtDNA was amplified by performing the 28-plex polymerase chain reaction (PCR). 186 genotypes of mtDNA polymorphisms were determined (G&G Science Corporation, Fukushima, Japan) by a method that combines the PCR and sequence-specific oligonucleotide probes with the use of suspension array technology (Luminex® 100™; Luminex, Austin, TX, USA) [11]. Details of the methodology used for genotyping, including the primers and probes for haplotyping, were given previously [15]. To confirm the accuracy of genotyping by this method, we subjected 91 DNA samples whose entire sequence of the mitochondrial genome had been determined by direct sequencing to the Luminex method. In each instance, the genotype determined by the Luminex sequence-specific oligonucleotide hybridization assay system was identical to that determined by the direct sequencing. Based on these mtDNA polymorphisms, the mitochondrial haplotypes were classified into 2 macrohaplogroups (i.e., N and M) and 12 haplogroups (i.e., F, B, A, N9a, N9b, M7a, M7b, G1, G2, D4a, D4b, and D5).

Statistical analysis

All measurements and calculated values were expressed as the mean±SEM. We compared the mean values of background characteristics of the subjects and physical characteristics among mitochondrial macrohaplogroups and/or haplogroups by use of one-way analysis of variance (ANOVA) and analysis of covariance (ANCOVA). A *P*-value <0.05 was considered statistically significant. All statistical analyses were performed by use of JMP version 8 software (SAS Institute Japan, Tokyo, Japan).

Results

The background characteristics of the subjects who participated in the present study are shown in ○ **Table 1**. All of the background data were similar between mitochondrial macrohaplogroups N and M. The physical characteristics of the subjects are given in ○ **Table 2**. When we analyzed the 2 major Japanese macrohaplogroups, N and M, leg extension power (1.12±0.04 vs. 1.03±0.03 kilowatts, $P=0.0395$), leg extension power based on body weight (18.3±0.5 vs. 17.1±0.3 watts/kg body weight, $P=0.0343$), and height of the vertical jump (38.0±0.9 vs. 36.0±0.6 cm, $P=0.0485$) were significantly higher in the subjects with mitochondrial macrohaplogroup N than in those with macrohaplogroup M; whereas hand grip strength was similar between the 2 groups. After adjustment of age as covariant, these 3 parameters: leg extension power, leg extension power based on body weight, and height of the vertical jump, were not significantly different between macrohaplogroups N and M ($P\geq0.05$ by ANCOVA), although these parameters tended to be different between the 2 groups. All of the other parameters, i.e., step count, physical activity, VO_2peak, HRmax, fat mass, % fat, fat-free mass (FFM), appendicular FFM, and relative skeletal muscle index (RSMI) were similar between subjects with mitochondrial macrohaplogroup N and those with macrohaplogroup M (○ **Table 2**).

When we divided subjects into 2 groups: i.e., males and females, height of the vertical jump for men (49.0±1.1 vs. 45.8±0.9 cm, $P=0.0291$ by ANOVA) was significantly higher in the subjects with mitochondrial macrohaplogroup N than in those with macrohaplogroup M. Even after adjustment of age as covariant, this trend was similar between macrohaplogroups N and M ($P=0.0251$ by ANCOVA). For women, all of the measured parameters were similar between macrohaplogroups. However, trends were similar in combined group of men and women.

When we analyzed the 12 mitochondrial haplogroups (i.e., F, B, A, N9a, N9b, M7a, M7b, G1, G2, D4a, D4b, and D5), all of the measured parameters were similar among these haplogroups (Data not shown).

Discussion

The main purpose of the present study was to examine the possible association between mitochondrial DNA polymorphisms and/or mitochondrial haplogroups and physical performance

phenotypes such as VO_2peak, muscle power, and muscle mass. Although the mitochondrial macrohaplogroups were not related to VO_2peak and muscle mass, macrohaplogroup N was significantly associated with stronger leg extension power and higher vertical jump performance compared with macrohaplogroup M for these Japanese adults, especially, in men. These differences in the leg extension power and vertical jump were not due to the differences in the step count or physical activity level.

The greater diversity of mtDNA sequences among African populations suggests that the most recent ancestor of modern humans (the so-called "mitochondrial Eve") originated from Africa [6,19]. As such, each of the African haplogroups (L0-L3) has deep genetic roots. Haplogroup L3 is proposed to be the ancestor of all non-African populations. European haplogroups (H, I, J, K, S, T, U, V, W, etc.) belong to macrohaplogroup N [34], whereas Asian haplogroups belong to both macrohaplogroups N and M (haplogroups A, B, F, and N9 to macrohaplogroup N; and haplogroups M7a, M7b, M8, D, and G to macrohaplogroup M) [32]. Both macrohaplogroups N and M have a common root with haplogroup L3 [1].

Mitochondrial macrohaplogroup N is characterized by 5 polymorphisms: m.8701A>G, m.9540T>C, m.10398A>G, m.10873T>C, and m.15301G>A, in the mtDNA [32]. 2 of these polymorphisms, namely, m.8701A>G and m.10398A>G, are nonsynonymous substitutions. These respective polymorphisms cause the Thr59Ala replacement in the ATPase subunit 6 (ATP6) gene and the Thr114Ala replacement in nicotinamide adenine dinucleotide (NADH) dehydrogenase subunit 3 (ND3) gene, which are subunits of the Complex V and I of the mitochondrial OXPHOS system, respectively. On the other hand, mitochondrial macrohaplogroup M is characterized by 5 other polymorphisms: m.303insC, m.489T>C, m.10400C>T, m.14783T>C, and m.15043G>A [32]. 2 of them, namely, m.303insC and m.489T>C, are located in the major non-coding region. Although the other 3 polymorphisms, namely, m.10400C>T, m.14783T>C, and m.15043G>A, are located in the protein-coding region, none of these polymorphisms characterizing macrohaplogroup M cause an amino acid replacement. Therefore, functional differences between macrohaplogroup N and M are ascribable to 2 polymorphisms: m.8701A>G (ATP6: Thr59Ala) and m.10398A>G (ND3: Thr114Ala), which are specific to mitochondrial macrohaplogroup N. It is reasonable to speculate that these Thr-to-Ala amino acid replacements are accompanied by functional alterations of the OXPHOS system.

The main function of mitochondria is to produce ATP by OXPHOS. We previously reported that certain mitochondrial haplogroups in Japanese individuals are associated with metabolic disorders closely related to mitochondrial function, such as obesity [14], type 2 diabetes mellitus [13,15,17], and metabolic syndrome [13,33]. Furthermore, we reported that certain mitochondrial DNA polymorphisms and/or mitochondrial haplogroups in Kenyan and Japanese populations are associated with elite endurance athlete status related to mitochondrial aerobic capacity [24,30]. Thus, it is generally believed that mitochondrial function is related to aerobic performance phenotypes, but not anaerobic performance phenotypes. Interestingly, mitochondrial macrohaplogroup N was associated with muscle power such as leg extension power and vertical jump performance in the present study.

Previous studies also focused on the roles of mitochondria in the regulation of intracellular calcium dynamics [10,21]. Calcium regulates muscle contraction. During activation of contraction in skeletal muscle, calcium is released from the sarcoplasmic reticulum. Mitochondria can transiently store calcium, a contributing process for homeostasis in the cell of calcium. We previously reported that the baseline mitochondrial calcium levels and peak cytosolic calcium levels after stimulation with histamine, which induces the release of calcium from the sarcoplasmic reticulum, are higher in cybrids with mitochondrial macrohaplogroup N than in those with mitochondrial macrohaplogroup M [20]. Thus, a certain mitochondrial macrohaplogroup might be related to intracellular calcium dynamics. In addition, mitochondria may play an important role in determining muscle fiber type composition. Because it was previously reported that peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PPARGC1A) and/or PPAR-delta (PPARD), a regulator of mitochondrial biogenesis, drives the ratio of slow/fast-twitch muscle fibers [22,35]. If certain haplogroup-related polymorphisms in the mtDNA down-regulate mtDNA replication and/or transcription by PPARs or own its variation, muscle composition can be changed to fast-twitch muscle fiber. Thus, a certain mitochondrial macrohaplogroup, which indicates differences in mitochondrial function, may influence anaerobic performance phenotypes such as muscle power. Further studies are necessary to conclude that mitochondria play an important role in calcium dynamics and in determining muscle fiber type composition.

Interestingly, we previously reported that mitochondrial haplogroup F is associated with elite Japanese "sprint/power" athlete status [24]. The haplogroup F is one of the major components of macrohaplogroup N [32], which was associated with muscle power in the present study. Although we could not demonstrate a significant association between mitochondrial haplogroup F and anaerobic performance phenotypes, both leg extension power (18.3±1 vs. 17.3±0.3 watts/kg body weight) and vertical jump performance (38.2±1.9 vs. 36.5±0.5 cm) tended to be higher in subjects with mitochondrial haplogroup F than in those with other haplogroups in the present study. On the other hand, neither mitochondrial macrohaplogroups nor haplogroups were associated with parameters of muscle mass, such as FFM, appendicular FFM, and RSMI, in the present study. Therefore, mitochondrial function might influence muscle quality, but not muscle volume.

In conclusion, we found a significant association between mitochondrial macrohaplogroup N and anaerobic performance phenotypes such as leg extension power and vertical jump performance in Japanese individuals, especially, in men. This association may implicate this mitochondrial macrohaplogroup in determining muscle performance in the Japanese population. However, we could not find any associations between mitochondrial haplogroups and muscle power, when we analyzed 12 Japanese major mitochondrial haplogroups. It should be noted that the sample size of the present study was relatively small, especially as we had divided the subjects into 12 mitochondrial haplogroups. Further extensive studies are necessary to understand the functional link between mitochondrial macrohaplogroups and/or haplogroups and muscle power.

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ORIGINAL ARTICLE

Adverse effects of coexistence of sarcopenia and metabolic syndrome in Japanese women

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BACKGROUND/OBJECTIVES: Little information is available regarding the interactions of sarcopenia and metabolic syndrome (MetS) in the risks of these age-associated diseases in women. The present cross-sectional study was performed to investigate whether the coexistence of sarcopenia and MetS further increases the risks of lifestyle-related diseases in Japanese women.
SUBJECTS/METHODS: Healthy Japanese women ($n = 533$) aged 30–84 participated in this study. MetS was defined as higher body mass index, fasting plasma glucose, systolic or diastolic blood pressure and blood lipid abnormalities. Appendicular muscle mass and bone mineral density (BMD) were measured using dual-energy X-ray absorptiometry. The criterion of low muscle mass and strength defined median skeletal muscle index (appendicular muscle mass/height^2, kg/m^2) and handgrip strength.
RESULTS: Two-way ANCOVA with adjustment for age, body fat percentage and whole-body lean tissue mass indicated that sarcopenia and MetS interacted to produce a significant effect on HbA1c, systolic blood pressure, triglycerides and brachial-ankle pulse wave velocity in Japanese women. The systolic blood pressure, triglycerides and brachial-ankle pulse wave velocity were significantly higher in women with coexisting sarcopenia and MetS than in healthy controls or in those with sarcopenia or MetS alone. The HbA1c in the coexisting sarcopenia and MetS group was higher than in healthy controls and sarcopenia subjects.
CONCLUSIONS: The coexistence of sarcopenia and MetS further increases the risks of cardiovascular diseases, such as type 2 diabetes mellitus, hypertension, arterial stiffness and hyperlipidemia even adjustment of age and body composition in adult Japanese women.

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Keywords: body composition; bone mineral density; cardiorespiratory fitness; CVD risk factors; metabolic syndrome; sarcopenia

INTRODUCTION

Sarcopenia, a reduction in muscle mass and muscle strength with age, causes impaired gait,[1] disability,[2] falls[3] and osteoporosis,[4–6] and increases the risk of developing a wide range of chronic disorders, including hypercholesterolemia, atherosclerosis, hyperglycemia, insulin resistance and hypertension.[7–10] On the other hand, it is well known that metabolic syndrome (MetS), which generally increases with advancing age, is also associated with increased risk of vascular events,[11] ischemic stroke[12] and type 2 diabetes mellitus.[13] Although the causes of sarcopenia are not yet clearly understood, catabolic stimulation (subclinical inflammation and production of catabolic cytokines) of muscle has been investigated as a potential mechanism of sarcopenia.[14] Thus, the causes of sarcopenia and MetS, which are associated with abnormal adipocytokine secretion, partly overlap. However, the interaction between sarcopenia and MetS on the risks of cardiovascular diseases (CVD) has not been investigated in detail.

Many investigators have shown that muscle strength[15–18] and muscle mass[4,19,20] are associated with site-matched bone mineral density (BMD). Walsh *et al.*[4] established that the prevalence of sarcopenia was 12.5% in premenopausal osteopenic women, while in postmenopausal women, the value was 25% for those with osteopenia and 50% for those with osteoporosis. Previous studies showed that vertebral BMD was significantly lower in women with MetS among 2475 Korean women after adjustment for age, weight and height,[21] and the incidence of osteoporotic non-vertebral fractures was higher in women with MetS in the Rancho Bernardo Study.[22] Therefore, although BMD may be associated with both sarcopenia and MetS, it has not been determined whether the interaction between sarcopenia and MetS further increases total and regional BMD as determined by dual-energy X-ray absorptiometry (DXA).

We hypothesized that the coexistence of sarcopenia and MetS causes further increases in the risks of lifestyle-related diseases, including CVD and osteoporosis, in adult women. The present cross-sectional study was performed to investigate whether the coexistence of sarcopenia and MetS causes further increases in the risks of lifestyle-related diseases in adult Japanese women.

MATERIALS AND METHODS

Subjects

Healthy Japanese women ($n = 533$) aged 30–84 years participated in this study; these were the same subjects as included in our previous study.[9] The distribution of age categories of subjects were 11.4% ($n = 61$) of <39yrs, 21.2% ($n = 113$) of <49 yrs, 25.9% ($n = 138$) of <59 yrs, 29.8% ($n = 159$) of <69 yrs and 11.6% ($n = 62$) of <85 yrs, respectively. Subjects were recruited from the community around the National Institute of Health and Nutrition (Tokyo, Japan). All subjects were free of overt CVD and stroke, as determined using a medical history questionnaire. The subjects were not taking any medications, such as beta-blockers, steroids or hormone replacement therapy. All subjects were free of any overt signs or symptoms of chronic disease. They were sedentary or moderately active,

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and participated in a swimming, stretching and 'healthy gymnastics' program; however, none of the subjects participated in other vigorous sports activities. The purpose, procedures and risks of the study were explained to all participants before inclusion, and all subjects gave their written informed consent before enrolling in the study. The study was performed in accordance with the guidelines of the Declaration of Helsinki and was approved by the Human Research Committee of the National Institute of Health and Nutrition, Tokyo, Japan. Body weight and height were recorded, and body mass index was calculated as weight in kilograms divided by the square of the height in meters. Systolic blood pressure, diastolic blood pressure and mean blood pressure were measured at rest using a vascular testing device (Form PWV/ABI; Colin Medical Technology, Tokyo, Japan). Chronic arterial blood pressure levels at rest were measured with the same device over the brachial and dorsalis pedis arteries. Recordings were made in triplicate with subjects in the supine position. The brachial-ankle pulse wave velocity (baPWV), which provides qualitatively similar information to that derived from central arterial stiffness,[23] was measured by the volume plethysmographic method.

Analysis of blood samples

All blood samples were drawn with the subject in the seated position. Fasting (>12 h) blood samples were collected by venipuncture in tubes with or without ethylenediamine tetraacetic acid (for plasma or serum). The blood samples were centrifuged at 1500 r.p.m. for 15 min and stored at −20 °C. Serum concentrations of triglycerides were determined by commercial kits (Mitsubishi Chemical Medience, Tokyo, Japan). Serum high-density lipoprotein (HDL)-cholesterol was measured by an enzymatic method (Mitsubishi Chemical Medience). Fasting plasma glucose was measured by the glucose dehydrogenase method. Whole-blood glycohaemoglobin A1c (HbA1c) was measured by an enzymatic method (Glycohemoglobin A1c kit; Mitsubishi Chemical Medience).

As waist circumference data were not available, the following risk factors of MetS (highest value = 4) were used: (1) body mass index $\geqslant$25 kg/m^2; (2) blood pressure $\geqslant$130 mm Hg systolic and/or $\geqslant$85 mm Hg diastolic; (3) triglycerides $\geqslant$150 mg/dl and/or HDL-cholesterol $\leqslant$40 mg/dl; and (4) fasting plasma glucose $\geqslant$110 mg/dl. The body mass index value was shown previously to be a useful predictor of the presence of multiple metabolic risk factors similar to waist circumference in middle-aged Japanese subjects.[24] The definition of MetS was high body mass index plus one or more of the other risk factors. Recently, previous studies have commonly used these criteria and definition of MetS in Japan.[25,26]

Measures of whole-body DXA

Lean soft tissue mass and BMD were determined for the whole body by DXA (Hologic QDR-4500A scanner; Hologic, Waltham, MA, USA). Participants were positioned for whole-body scans in accordance with the manufacturer's protocol. Participants lay in the supine position on the DXA table with the limbs close to the body. The whole-body lean soft tissue mass was divided into several regions, that is, the arms, legs and trunk. Body composition was determined by Hologic software version 11.2:3 for windows (Hologic). A recent investigation indicated that the definition of sarcopenia was based on documentation of criterion low muscle mass plus low muscle strength.[27] Therefore, the criterion of low muscle mass defined median SMI value of 6.70 kg/m^2 in this study subjects. On the other hands, low muscle strength was defined by low handgrip strength, and the cutoff value of handgrip strength was defined as values one standard deviation (s.d.) below the mean of handgrip strength obtained in this study from younger adults aged 30–49. The mean ± s.d. of handgrip strength were 29.8 ± 5.4 and cutoff value was 24.4 kg. Previous study demonstrated <20 kg of the handgrip strength for the cutoff value.[28] In the present study, there is no information of the cutoff value of sarcopenia-involved muscle strength in Japanese population.

Measures of fitness

The maximum oxygen uptake (VO_2max) was measured by incremental exercise testing using a cycle ergometer. Incremental cycle exercise began at a work rate of 90 W (60 r.p.m.), and power output was increased by 30 W/min until the subjects could not maintain the fixed pedaling frequency. During the ergometer test, the subjects were encouraged to exercise at as high intensity as possible. 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 meter (NDS-2A-T; Shinagawa Dev., Tokyo, Japan). The highest value of VO_2 during the exercise test was designated as VO_2max. Handgrip strength of the right upper limb was measured using a handheld dynamometer. In the standing position, with the arms straight by the sides, the subject gripped the dynamometer as hard as possible for 3 s without pressing the instrument against the body or bending at the elbow. Values (kg) were recorded as the averages of two trials. Leg extension power was measured with an isokinetic leg power system (Anaero Press 3500; Combi Wellness, Tokyo, Japan) in the sitting position. Flexibility was measured by a sit-and-reach test using a digital flexibility testing device (T.K.K.5112; Takeikiki, Tokyo, Japan) after some stretching. The device displays the distance through which it has moved. Subjects sat on the floor with their hips, back and occipital region of the head touching a wall, and the legs held straight by the tester. They placed both hands on the device with the arms held straight. The zero point of the device was set in this position. They were then asked to bend forward slowly and reach as far forward as possible. The better of two trials was recorded.

Statistical analysis

We compared the mean values of physical characteristics, body composition, fitness and the risks of lifestyle-related diseases between healthy controls and sarcopenia or MetS groups by the unpaired Student's *t*-test. The proportions of sarcopenia and MetS were confirmed by the χ^2 test. In addition, we tested the influence of sarcopenia and MetS on the risks of lifestyle-related diseases by two-way ANCOVA with adjustment for age, body fat percentage and whole-body lean tissue mass as a covariate. When a significant difference was observed in the interaction, comparisons between groups were tested by the unpaired Student's *t*-test. Values are expressed as means ± s.e.m. In all analyses, $P<0.05$ was taken to indicate statistical significance.

RESULTS

Comparisons between subjects' characteristics and MetS risks in the subjects with sarcopenia and/or MetS and healthy control subjects are shown in Table 1. Body fat percentage was significantly higher in both sarcopenia and MetS women than in healthy controls ($P<0.01$). Whole-body and regional BMD in sarcopenia women were significantly lower than those in healthy controls ($P<0.001$). The leg extension power, handgrip strength and flexibility in sarcopenia women were significantly lower than those in healthy controls ($P<0.001$). The VO_2max in MetS women were significantly lower than those in healthy controls ($P<0.05$).

The χ^2 test indicated that the prevalence of sarcopenia was significantly higher in subjects without MetS (122/468, 26.1%) than in those with MetS (7/65, 10.8%, $P<0.01$). We tested the interaction of sarcopenia and MetS on subject's characteristics and MetS risks by two-way ANCOVA with adjustment for age, body fat percentage and whole-body lean tissue mass as a covariate (Table 2). The effects of the interaction between sarcopenia and MetS on systolic blood pressure, baPWV and HbA1c (Figure 1) were significant. The systolic blood pressure and baPWV in subjects with coexisting sarcopenia and MetS were significantly higher than those in subjects with either sarcopenia or MetS alone and in healthy controls. In addition, the effects of the interaction between sarcopenia and MetS on serum triglycerides level and triglycerides/HDL-cholesterol were significant. The triglycerides and triglycerides/HDL-cholesterol in the healthy controls were significantly lower than those in subjects with both sarcopenia and MetS or in those with either sarcopenia or MetS alone (Table 2). The interactions of sarcopenia and MetS on subject's body composition and fitness are shown in Table 3. The effects of the interaction between sarcopenia and MetS on fitness and both whole-body and regional BMD were not significant.

DISCUSSION

This cross-sectional study was performed to investigate whether the coexistence of sarcopenia and MetS causes further increases in the risks of lifestyle-related diseases, including CVD and

Table 1. Physical characteristics, body composition and fitness in sarcopenia and MetS in Japanese women

	Sarcopenia		*MetS*	
	Normal (non-sarcopenia)	*Class 1 sarcopenia*	*Normal (non-MetS)*	*MetS*
n (%)	404 (75.8%)	129 (24.2%)	468 (87.8%)	65 (12.2%)
Age (years)	53.1 ± 0.6	62.2 ± 0.9***	54.9 ± 0.6	57.7 ± 1.4
BMI (kg/m^2)	23.0 ± 0.2	21.6 ± 0.2***	21.9 ± 0.1	28.0 ± 0.4**
% BF	28.3 ± 0.3	30.2 ± 0.5**	27.7 ± 0.3	36.3 ± 0.4**
SBP (mm Hg)	120.2 ± 0.9	123.1 ± 1.7	118.3 ± 0.8	139.8 ± 2.5**
DBP (mm Hg)	71.6 ± 0.5	71.2 ± 0.9	70.1 ± 0.5	81.7 ± 1.4**
MBP (mm Hg)	91.8 ± 0.7	93.8 ± 1.3	90.2 ± 0.6	107.1 ± 1.8**
baPWV (cm/s)	1501 ± 248	1534 ± 324	1660 ± 322	1660 ± 322**
TG (g/dl)	88.3 ± 2.5	97.2 ± 6.2	81.3 ± 1.8	155.9 ± 12.1**
HDLC (mg/dl)	66.7 ± 0.8	69.7 ± 1.5	68.6 ± 0.7	58.5 ± 1.3**
TG/HDLC	1.46 ± 0.06	1.65 ± 0.16	1.31 ± 0.04	2.94 ± 0.31**
FPG (mg/dl)	94.3 ± 0.9	95.2 ± 1.4	92.6 ± 0.5	108.2 ± 4.3**
HbA1c (%)	5.10 ± 0.03	5.25 ± 0.06*	5.08 ± 0.02	5.55 ± 0.15**
Whole-body BMD (g/cm^2)	1.06 ± 0.01	0.95 ± 0.01***	1.03 ± 0.01	1.04 ± 0.01
Arm BMD (g/cm^2)	0.66 ± 0.00	0.59 ± 0.01***	0.65 ± 0.00	0.65 ± 0.01
Lumber spine BMD (g/cm^2)	1.02 ± 0.01	0.88 ± 0.01***	0.99 ± 0.01	0.99 ± 0.02
Leg BMD (g/cm^2)	1.08 ± 0.01	0.97 ± 0.01***	1.05 ± 0.01	1.08 ± 0.01
Total LSTM (kg)	40.7 ± 0.2	35.5 ± 0.3***	39.0 ± 0.2	42.5 ± 0.7**
Arm LSTM (kg)	3.7 ± 0.0	3.1 ± 0.0***	3.6 ± 0.0	3.7 ± 0.1
Trunk LSTM (kg)	19.8 ± 0.1	17.4 ± 0.1***	19.0 ± 0.1	21.2 ± 0.3**
Leg LSTM (kg)	13.3 ± 0.1	11.2 ± 0.1***	12.6 ± 0.1	13.6 ± 0.2**
AMM (kg)	17.0 ± 0.1	14.3 ± 0.1***	16.2 ± 0.1	17.3 ± 0.3**
SMI (kg/m^2)	6.88 ± 0.04	6.12 ± 0.04***	6.62 ± 0.03	7.28 ± 0.10**
Handgrip strength (kg)	28.5 ± 0.2	21.1 ± 0.2***	26.7 ± 0.2	26.3 ± 0.7
LEP (W)	847 ± 13	634 ± 17***	782 ± 12	859 ± 44
Sit and reach (cm)	38.6 ± 0.5	36.1 ± 0.9*	38.1 ± 0.5	36.4 ± 1.2
VO_2max (ml/kg/min)	29.8 ± 0.4	28.0 ± 0.8	30.2 ± 0.4	23.7 ± 0.7*

Abbrevitions: AMM, appendicular muscle mass; baPWV, brachial-ankle pulse wave velocity; %BF, body fat percentage; BMD, bone mineral density; BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDLC, high-density lipoprotein cholesterol; LEP, leg extension power; LSTM, lean soft tissue mass; MetS, metabolic syndrome; MBP, mean blood pressure; SBP, systolic blood pressure; SMI, skeletal muscle index; TG, triglycerides; VO_2max, maximal oxygen uptake. *$P<0.05$, **$P<0.01$, ***$P<0.001$ for the significant difference from the normal subjects using unpaired Student's *t*-test. Data are mean ± s.e.m.

Table 2. The relationships between sarcopenia and MetS to the risks of cardiovascular diseases in Japanese women

	Normal	*MetS*	*Sarcopenia*	*Sarcopenia and MetS*	P *MetS*	P *sarcopenia*	P *interaction*
n	346 (64.9%)	58 (10.9%)	122 (22.9%)	7 (1.3%)			
Age (yrs)$^{\#}$	52.3 ± 0.6	57.4 ± 1.5	62.2 ± 1.0	60.7 ± 3.7	0.450	0.171	0.201
BMI (kg/m^2)	22.1 ± 0.1	28.2 ± 0.4	21.3 ± 0.2	26.1 ± 0.5	0.269	0.848	0.925
% BF (%)$^{\#}$	27.0 ± 0.3	36.1 ± 0.4	29.7 ± 0.5	38.0 ± 1.5	0.249	0.567	0.902
SBP (mm Hg)	117.2 ± 0.8	138.1 ± 2.5*	121.3 ± 1.6*,†	154.0 ± 8.1*,†,¶	0.233	0.524	**0.009**
DBP (mm Hg)	70.0 ± 0.5	81.5 ± 1.5	70.5 ± 0.9	83.4 ± 3.9	0.599	0.782	0.125
MBP (mm Hg)	89.4 ± 0.7	106.4 ± 1.9	92.7 ± 1.2	113.6 ± 5.9	0.303	0.856	0.062
baPWV (cm/s)	1254 ± 12	1444 ± 33*	1401 ± 24*	1686 ± 93*,†,¶	0.466	0.447	**0.006**
TG (g/dl)	78.5 ± 2.0	146.7 ± 9.9*	89.5 ± 4.1*,†	231.7 ± 76.0*,†,¶	0.933	0.547	**0.000**
HDLC (mg/dl)	68.0 ± 0.8	58.9 ± 1.4	70.5 ± 1.6	55.6 ± 4.6	0.442	0.798	0.517
TG/HDLC	1.26 ± 0.05	2.67 ± 0.22*	1.45 ± 0.10*,†	5.13 ± 2.10*,†	0.782	0.422	**0.000**
FPG (mg/dl)	92.3 ± 0.6	106.1 ± 4.5	93.4 ± 1.1	125.6 ± 14.8	0.101	0.180	0.065
HbA1c (%)	5.04 ± 0.02	5.46 ± 0.14*	5.20 ± 0.05†	6.23 ± 0.72*,¶	0.224	0.775	**0.012**

Abbrevitions: baPWV, brachial-ankle pulse wave velocity; %BF, body fat percentage; BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDLC, high-density lipoprotein cholesterol; MetS, metabolic syndrome; MBP, mean blood pressure; SBP, systolic blood pressure; TG, triglycerides. $^{\#}P$ values are the significant effects by two-way ANCOVA (sarcopenia × MetS) with adjustment for the covariate of other two valuables. *$P<0.05$ for the significant difference from normal subjects. †$P<0.05$ for the significant difference from MetS subjects. ¶$P<0.05$ for the significant difference from sarcopenia subjects. Bold face indicates significance ($P<0.05$). When a significant difference was observed in the interaction, comparisons between groups were tested by the unpaired Student's *t*-test. Data are mean ± s.e.m. *P* values are the significant effects by two-way ANCOVA (sarcopenia × MetS) with adjustment for the covariate of age, body fat percentage and whole-body lean soft tissue mass.

osteoporosis, in adult Japanese women. The results indicated that sarcopenia and MetS interacted to produce significant effects on CVD risks, such as systolic blood pressure, baPWV, HbA1c, serum triglycerides level and triglycerides/HDL-cholesterol. These results suggest that the coexistence of sarcopenia and MetS leads to further increases in the risks of type 2 diabetes mellitus, hypertension, arterial stiffness and hyperlipidemia even adjustment of age and body composition in adult Japanese women.

The χ^2 test indicated that the prevalence of sarcopenia was significantly higher in subjects without MetS (122/468, 26.1%) than in those with MetS (7/65, 10.8%). Subjects with sarcopenia have a healthy appearance, because they are most often not undernourished. MetS is closely associated with CVD and type 2 diabetes mellitus[29] and therefore it has been the focus of governmental health promotion activities in developed countries. However, sarcopenia is less well understood among

the public, although many studies have shown that sarcopenia affects disability,[2] the risk of fractures[4–6] and a wide range of chronic disorders.[7–10] We confirmed that both sarcopenia and MetS are important factors that should be taking into account in governmental health promotion programs to regulate medical treatment costs.

Recently, it has been demonstrated that sarcopenia obesity is a new category of obesity in the elderly.[30] Central obesity directly affects inflammation, which in turn negatively affects muscle strength, contributing to the development and progression of sarcopenia obesity.[14] Therefore, proinflammatory cytokines may be critical in both the development and progression of sarcopenia obesity. Stephen and Janssen[31] reported that sarcopenia obesity, identified based on muscle strength but not muscle mass, was modestly associated with increased CVD risk. A community-based elderly cohort study in Korea in subjects aged 65 years or older showed that sarcopenia obesity, defined by appendicular muscle mass/body weight using DXA and visceral fat area exceeding 100 cm^2 on abdominal computed tomography, was more closely associated with MetS than either sarcopenia or obesity alone.[32] A longitudinal follow-up study of over 3000 older adults indicated that the combination of low muscle mass and abdominal obesity was not associated with an increased risk for the development of CVD over an 8-year follow-up period.[31] In addition, although the number of subjects in this study was relatively small, sarcopenic obese women have less risk factors predisposing them to CVD compared with obese postmenopausal women.[33] Thus, the results of previous studies regarding the relation between sarcopenia obesity and the risks of CVD are still controversial. Our results showed that the effects of the interaction between sarcopenia and MetS on systolic blood pressure, baPWV and HbA1c were significant (Table 2). The baPWV is a recognized indicator of arterial stiffness[34] and arterial compliance[35] and has been regarded as a marker reflecting vascular damage.[36] In addition, the effects of the interaction between sarcopenia and MetS on triglycerides and triglycerides/HDL-cholesterol were also significant in this study. The serum triglycerides level and triglycerides/HDL-cholesterol, which are indexes of atherosclerosis, were significantly lower in the healthy controls than in subjects with sarcopenia and MetS and in those with sarcopenia or MetS alone (Table 2). These results indicate that it is desirable to remain without sarcopenia and MetS for the prevention of type 2 diabetes mellitus, hypertension, arterial stiffness and hyperlipidemia in adult women.

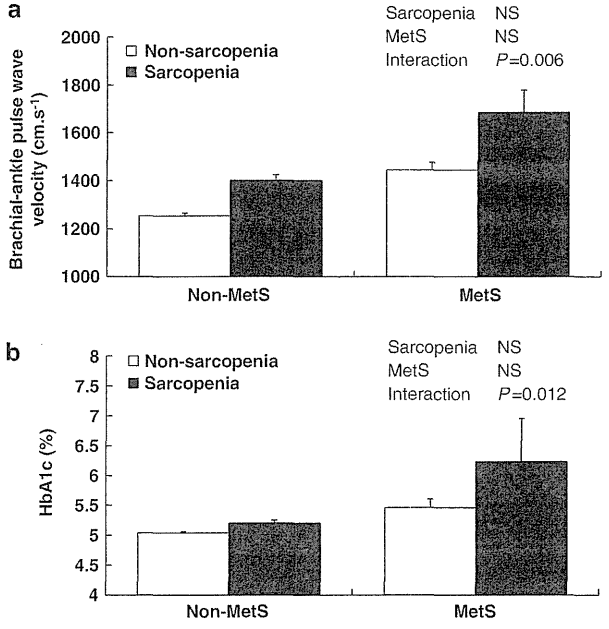

Figure 1. Interaction between sarcopenia and metabolic syndrome (MetS) with respect to brachial-ankle pulse wave velocity (**a**) and whole-blood glycohaemoglobin A1c (**b**) in adult Japanese women. The effects of sarcopenia and MetS and their interaction were assessed by two-way ANCOVA with adjustment for age, body fat percentage and whole-body lean tissue mass as a covariate. Data are expressed as means ± s.e.m.

Previous studies showed that subjects with MetS had increased femoral neck BMD compared with controls without MetS in a United States population-based study,[37] and MetS women showed higher BMD than controls, mainly driven by their higher body weight, but bone remodeling was lower in these women.[38] Hernandez *et al.*[38] reported that despite the greater bone mass and lower bone turnover, fracture prevalence was not reduced, suggesting poorer bone quality and/or a higher tendency to fall. On the other hand, the mean vertebral BMD was significantly lower in subjects with MetS after adjustment for age, weight and height among 2475 Korean women.[21] Hwang and Choi[21] suggested that these two conflicting results may have been due to differences in subjects (race, age and comorbid disease status), adjusting covariates (especially menopause in women), samples used (non-fasting serum) and methods of analysis.

Many investigators have shown that muscle strength[15–18] and muscle mass[4,19,20] are associated with site-matched BMD. Walsh *et al.* reported that the prevalence rates of sarcopenia were 25% and 50% in postmenopausal women with osteopenia and with osteoporosis, respectively.[4] However, it is not clear whether the coexistence of sarcopenia and MetS causes further increases in total and regional BMD. In the present study, the effects of the interaction between sarcopenia and MetS on whole-body, arm and trunk BMD were not significant. However, there was significant difference in the whole-body and regional BMD

Table 3. *The relationships between sarcopenia and MetS to the BMD and fitness in Japanese women*

	Normal	*MetS*	*Sarcopenia*	*Sarcopenia and MetS*	P *MetS*	P *sarcopenia*	P *interaction*
Whole-body BMD (g/cm^2)	1.06 ± 0.01	1.05 ± 0.01	0.95 ± 0.01	1.00 ± 0.03	0.480	0.492	0.667
Arm BMD (g/cm^2)	0.67 ± 0.00	0.65 ± 0.01	0.59 ± 0.01	0.63 ± 0.02	0.466	0.662	0.358
Lumbar spine BMD (g/cm^2)	1.03 ± 0.01	0.98 ± 0.02	0.87 ± 0.01	1.03 ± 0.07	0.214	0.058	0.083
Leg BMD (g/cm^2)	1.08 ± 0.01	1.08 ± 0.01	0.97 ± 0.01	1.03 ± 0.03	0.380	0.160	0.695
Handgrip strength (kg)	28.8 ± 0.2	26.9 ± 0.7	21.1 ± 0.3	21.5 ± 0.4	0.759	0.419	0.315
LEP (W)	841 ± 13	876 ± 49	628 ± 18	727 ± 50	0.486	0.528	0.087
Sit and reach (cm)	38.9 ± 0.6	36.8 ± 1.1	36.3 ± 0.9	30.2 ± 8.7	0.838	0.100	0.838
VO_2max (ml/kg/min)	30.6 ± 0.4	23.7 ± 0.7	28.2 ± 0.9	24.0 ± 2.8	0.860	0.081	0.096

Abbrevitions: BMD, bone mineral density; LEP, leg extension power; MetS, metabolic syndrome; VO_2max, maximal oxygen uptake. Data are mean ± s.e.m. *P* values are the significant effects by two-way ANCOVA (sarcopenia × MetS) with adjustment for the covariate of age, body fat percentage and whole-body lean soft tissue mass. The effects of the interaction between sarcopenia and MetS on fitness or both whole-body and regional BMD were not significant.

between the normal and sarcopenia subjects but not between the normal and MetS subjects. These results suggest that the BMD in adult women has an impact on sarcopenia more than MetS.

Previous studies regarding the relationship between cardiorespiratory fitness and MetS suggested that a low level of physical fitness is a strong determining factor in the prevalence of MetS.[39–43] Lakka *et al.*[41] suggested that a sedentary lifestyle and especially low cardiorespiratory fitness measured by VO_2max are not only associated with MetS but could also be considered features of MetS. On the other hand, skeletal muscle mass directly affects to individual VO_2max level regardless of upper and lower extremity exercise,[44] and sarcopenia is associated with age-related loss of VO_2max among healthy people across the adult age range.[45] It is not understood how the interaction of sarcopenia and MetS causes further decreases in the age-related loss of cardiorespiratory fitness or muscle power. The results of this study showed that the effect of the interaction between sarcopenia and MetS on VO_2max was not significant. However, there was significant difference in the VO_2max between the normal and MetS subjects but not between the normal and sarcopenia subjects. These results suggest that the cardiorespiratory fitness in adult women has an impact on MetS more than sarcopenia.

The present study has several limitations. First, the observations of this study are tempered by the limitations inherent to cross-sectional studies. Previous study suggest that cross-sectional studies underestimate true aging loss in muscle size and strength.[46] Second, we do not have the data of insulin resistance, therefore we evaluated the risk of type 2 diabetes mellitus only in HbA1c, which could be a common mechanism behind both sarcopenia and MetS. This point is also one of the limitations in this study.

CONCLUSION

The findings of the present study indicated that the coexistence of sarcopenia and MetS further increases the risks of CVD, such as type 2 diabetes mellitus, hypertension, arterial stiffness and hyperlipidemia even adjustment of age and body composition in adult Japanese women. It is important to prevent both sarcopenia and MetS for public health and to prevent the development of CVD.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ORIGINAL RESEARCH

Increased Muscle Size and Strength From Slow-Movement, Low-Intensity Resistance Exercise and Tonic Force Generation

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The authors investigated the effects of low-intensity resistance training on muscle size and strength in older men and women. Thirty-five participants (age 59–76 yr) were randomly assigned to 2 groups and performed low-intensity (50% of 1-repetition maximum) knee-extension and -flexion exercises with either slow movement and tonic force generation (LST; 3-s eccentric, 3-s concentric, and 1-s isometric actions with no rest between repetitions) or normal speed (LN; 1-s concentric and 1-s eccentric actions with 1-s rests between repetitions) twice a week for 12 wk (2-wk preparation and 10-wk intervention). The LST significantly increased thigh-muscle thickness, as well as isometric knee-extension and -flexion strength. The LN significantly improved strength, but its hypertrophic effect was limited. These results indicate that even for older individuals, the LST can be an effective method for gaining muscle mass and strength.

Keywords: muscle hypertrophy, sarcopenia, aging

Sarcopenia, defined as the aging-related loss of muscle mass (Evans, 1995), results in a loss of strength and leads to a successive impairment of basic locomotory function. In older individuals, the loss of muscle strength has been shown to be a primary factor of frailty, falls, and loss of independence (Wolfson, Judge, Whipple, & King, 1995). Therefore, preventing sarcopenia is important to maintain the quality of life of older individuals.

Resistance training with moderate to high intensity (~80% one-repetition maximum [1RM]) has been extensively used to increase muscle mass and strength, while that with an intensity lower than 65% 1RM is considered less effective (McDonagh & Davies, 1984). The importance of training intensity has been thought to be consistent across age, as well as sex. In fact, some studies have shown that high-intensity

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