

コンドリア新生が高まるとの報告や、健康な人によるカロリー制限が筋ミトコンドリア新生を増強するとの報告を根拠として、カロリー制限がミトコンドリア新生を高めるとの考えは、広く受け入れられており、そのことが加齢の抑制や疾患の予防に対するカロリー制限の有効性を説明する理由とされてきている。しかし、身体の諸組織のミトコンドリアはエネルギー需要やエネルギー基質の供給の増減にตอบสนองして適応的に変化するということを考えると、このような現象はいささか不可思議である。

そこで、詳細な動物実験による検討が行われた¹⁰⁾。その結果、30%カロリー制限はPGC-1 α に加えて、ミトコンドリアに局在する諸酵素のたんぱく量と活性の測定により、骨格筋を含む身体諸器官のミトコンドリアを増加させないことが明らかになった。

5. カロリー制限がさまざまなモデル生物の寿命や健康に及ぼす影響

Fontanaら¹¹⁾は酵母からヒトに至るさまざまなモデル生物を対象として、寿命や健康に及ぼすカロリー制限の効果について総説を執筆している。それによると、カロリー制限による寿命や健康への影響はモデル動物によって大きく異なっている。ヒトにおける長期にわたるカロリー制限の影響は寿命の延長については、肥満、糖尿病、高血圧を予防し、癌や心臓病のリスクを低減することは明らかであるが、未だ解明されていないことも多く、今後の更なる研究が望まれる。また、この総説には酵母、線虫、ハエ、そして哺乳類に至る多様なモデル生物の寿命を制御している栄養シグナル経路が提示されており、食事制限は直接的に(酵母)、あるいはIGF-1レベルの低下を介して間接的に(線虫、ハエ、哺乳類)シグナル伝達経路の活性を低下させるとされている。さらに、加齢を促進するTORやS6Kは酵母、線虫、ハエ、そしてマウスにも保持されており、それらの機能についても記述されている。寿命を延長させる詳細な代謝的メカニズムについては以下のサイトを参照されたい(www.sciencemag.org/cgi/content/full/328/5976/321)。

おわりに一人の“健康・長寿”とライフスタイル

平成22年国民健康・栄養調査結果の概要(厚生労働省, 2012)によると、全国平均で20~60歳代の男性の肥満者(BMI 25以上)の割合は男性が30%程度で推移しており、40~60歳代の女性では22%程度であった(女性では20歳代のやせの者の割合が急増している)。しかし、同調査結果は生活習慣病の予防・改善を目的とした生活習慣の改善に取り組んでいる者も多いことを報告している。生活習慣病の予防・改善を目的とした生活習慣の改善に取り組んでいる者(30歳以上)の割合は、男性50%、女性58%であり、そのために普段の生活で心がけている内容は、男性では“食べ過ぎないようにしている(カロリー制限している)”(47%)が最も多く、以下、“野菜をたくさん食べるようにしている”(45%)、“脂肪(あぶら分)をとりすぎないようにしている”(39%)、“運動をするようにしている”(39%)が続いていた。一方、女性では、“野菜をたくさん食べるようにしている”(58%)が最も高く、“脂肪(あぶら分)をとりすぎないようにしている”(52%)、“食べ過ぎないようにしている(カロリー制限している)”(51%)がほぼ同じで高くなっていった。これらのことが継続的に実践され、中高年者が健康増進を図ることが強く望まれる。

ところで、カナダのWillcox兄弟と鈴木信博士の共著による“The Okinawa Program”が“オキナワ式食生活革命”(飛鳥新社, 2004)として翻訳出版され、“長寿王国・オキナワ”が世界的に注目されてから10年近くが経過した。そのなかで筆者らは「沖縄プログラムは、(中略)食事だけでも健康に長生きする強力な処方箋になる。植物性食品主体の低カロリーの食事は、アメリカの国立がん研究所(NCI)が勧めている食事と合致しているだけでなく、それよりさらに進んでいるし、アメリカのほかの科学的、医学的権威の多くが勧告している規準を上回っている。それは心臓病、がん、脳卒中を含めて老化が関連する多くの病気を防ぐ食事であり、生涯スリムで健康でありたいと願っている人には絶好のチャンスを与えてくれる」と

述べている。しかし、一方で、“沖縄が長寿でなくなる日”（沖縄タイムス「長寿」取材班編，岩波書店，2004）の冒頭では「沖縄県の働き盛り男性の死亡率は全国で最悪。厚生労働省が発表した2000年の年齢階級別死亡率には，ショッキングな数字が並ぶ。35歳から44歳の死亡率は最も高く，50歳以下は軒並み全国平均を上回る。また男性の平均寿命は，1980年，85年には全国1位の座にあったものの，90年は5位，95年は4位となり，2000年は26位に急落した」ことが記載されている。沖縄が本土に復帰して今年（2012年）で40年である。平成22年国民健康・栄養調査結果の概要（厚生労働省，2012）も示しているように，男性（20～69歳）の肥満者（BMI：25以上）の割合は沖縄県が45.2%でワーストワン（全国平均31.1%）であり，歩数に関しても，20歳以上の男性が18位（7,214歩）で全国平均（7,225歩）と同レベルであり，女性では36位（5,823歩）と全国平均（6,287歩）をかなり下回っている。日常の食事と運動が影響するカロリー（エネルギー）の出納と肥満，健康・長寿という視点から，沖縄県の今後の健康指標の推移が注目される。

これまでの研究や調査による報告から，カロリー過多による肥満が健康，寿命にネガティブな影響を及ぼすことは明らかであり，適切なカロリー制限と運動による十分なエネルギー消費が，健康・長寿に不可欠であることが，本稿で示したデータによって理解される。

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Associations between muscular fitness and metabolic syndrome: Cross-sectional study of Japanese women and men

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ABSTRACT

Metabolic syndrome (MetS) is a complex inter-related risk factor for cardiovascular disease and type 2 diabetes mellitus. High cardiorespiratory fitness is known to contribute to prevention of MetS. However, little is known regarding the association between muscular fitness and MetS in Japanese adults. The purpose of this study was to examine the associations between muscular fitness and MetS in Japanese women and men. This cross-sectional study included 335 women and 209 men aged 30 - 79 y. MetS was determined according to the 2009 criteria of the International Diabetes Federation. Muscular fitness was evaluated by muscular fitness composite score (MFS), which was determined using Z scores from grip strength and sit-ups. Participants were classified by MFS tertile into low, middle, and high MFS groups. We used multiple logistic regression analysis to estimate odds ratios for the incidence of MetS in each group. The prevalence of MFS was 27.2% in women and 27.3% in men. Adjusted odds ratios for MetS prevalence in the low, middle, and high MFS groups, after adjusting for age, smoking status, alcohol intake, and exercise habits, were 1.0 (referent), 0.90 (95% confidence interval [CI], 0.50 - 1.62), and 0.49 (95% CI, 0.25 - 0.94; *P* for trend = 0.03) in women; in men, they were 1.0 (referent), 0.49 (0.23 - 1.04), and 0.42 (0.18 - 0.97; *P* for trend = 0.04), respectively. Muscular fitness is inversely associated with the prevalence of MetS in Japanese women and men.

Keywords: Muscle Strength; Muscle Endurance; Muscular Fitness; Metabolic Syndrome

1. INTRODUCTION

Metabolic syndrome (MetS) is a clustering of central obesity and cardiovascular disease (CVD) risk factors, including abnormal blood pressure, lipids, and blood glucose [1]. Insulin resistance occurring as a result of visceral fat accumulation is a key factor in MetS and is considered a strong predictor of CVD events [2]. Over the past 2 decades, the prevalence of MetS has increased in Japan as well as in Western countries. Because individuals with MetS have an elevated risk of developing type 2 diabetes [3,4] and CVD [5,6], strategies to prevent an epidemic of this syndrome are urgently required [7].

The primary management approach for MetS is healthy lifestyle promotion such as increased physical activity and diet modification [8]. Because physical fitness (*i.e.*, cardiorespiratory fitness [CRF] and muscular fitness) is primarily determined by physical activity, high physical fitness is thought to be effective for improving MetS. Previous studies have demonstrated an inverse association between CRF and MetS prevalence and suggested that CRF is an independent predictor of MetS incidence [9-11]. Compared with CRF, fewer studies have been conducted on the association between muscular fitness and MetS. While an inverse relationship between muscular strength and MetS has been previously illustrated in American [12,13], Australian [14], and European populations [15], this relationship has not been well studied in populations of Japanese adults [16-18], especially Japanese women. The purpose of this study was to examine the associations between muscular fitness and MetS in Japanese women and men.

2. METHODS

2.1. Subjects

The subjects were 335 women and 209 men, aged 30 -

79 y, who underwent a baseline preventive medical examination and physical fitness tests between 2006 and 2010 and were recruited to participate in a training program for health promotion at Fujisawa City Health and Medical Center. All subjects provided written informed consent before enrollment in the study. This study was approved by the Ethics Committee of Waseda University and conducted in accordance with the spirit of the Declaration of Helsinki.

2.2. Clinical Examination

All subjects received preventive medical examinations at the medical institution in Fujisawa City. The exam included a measurement of height, body weight, waist circumference (WC), blood chemistry analyses (triglycerides, TG; high-density lipoprotein, HDL-c; fasting blood glucose, FPG), and resting blood pressure (BP; systolic blood pressure, SBP; diastolic blood pressure, DBP). Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m²), and WC was measured at the umbilicus with subjects in the standing position.

2.3. Criteria for MetS

MetS was defined as meeting 3 or more of the following criteria [19]: abdominal obesity (WC \geq 80 cm in women, WC \geq 90 cm in men); high TG (\geq 150 mg/dL or taking medicine to lower TG); low HDL-c ($<$ 50 mg/dL in women, $<$ 40 mg/dL in men); high BP (SBP \geq 130 mmHg or DBP \geq 85 mmHg, or taking medicine to lower BP); and high FPG (\geq 100 mg/dL or taking medicine to lower FPG).

2.4. Muscular Fitness

Grip strength test, used as a proxy for overall strength [20], was assessed using a handgrip dynamometer (ED-D100PNR, Yagami, Nagoya, Japan) [21]. The subject stood with the arm completely extended and squeezed the dynamometer with maximum isometric effort. Grip strength was measured twice on each side. The best of the 4 grip measurements was used to characterize maximum muscle strength. To account for differences in body size, total handgrip was adjusted for body weight (kg).

Abdominal muscle endurance was evaluated by a sit-up test [21]. The subject started in a lying position with hands crossed over the chest, knees bent at a 90° angle, and heels and feet flat on the floor. The subject had to rise to a position with the elbows pointed forward until they touched the thighs. The total number of correctly performed and completed sit-ups within 30 s was counted.

Muscular fitness was evaluated by muscular fitness composite score (MFS), which was determined using Z

scores from grip strength and sit-ups.

2.5. Confounding Variables

Several confounding variables were included in the analyses: age (y), smoking status (current, former, never), daily alcohol intake (g/day), and exercise habits (never, once/wk, 2 - 3 times/wk, 4 - 5 times/wk, 6 - 7 times/wk). These variables were assessed by means of a questionnaire.

2.6. Statistical Analysis

Measured and calculated values are presented as mean \pm SD or number (%). Participants were classified by MFS tertile into low, middle, and high MFS groups. Analysis of variance was used for continuous variables with a normal distribution, the Kruskal-Wallis test was used for continuous variables with a non-normal distribution, and the chi-square test was used for categorical variables. The association of muscular fitness with the risk of having MetS was estimated using multiple logistic regression analysis adjusted for age (Model 1), and further adjusted for smoking status, alcohol intake, and exercise habits (Model 2). The data were analyzed with SPSS 19.0 for Windows (IBM Japan, Tokyo, Japan). The statistical significance level was set at $P < 0.05$.

3. RESULTS

Table 1 shows the characteristics of individuals according to MFS level. Women with the highest MFS demonstrated a significantly lower body weight, BMI, WC, SBP, DBP, and TG level ($P < 0.05$) and a higher Grip strength, Sit-ups, and HDL-c level ($P < 0.01$). Men with the highest MFS were significantly younger and had a lower body weight, BMI, WC, and TG level ($P < 0.05$) and higher Grip strength, Sit-ups, and HDL-c level ($P < 0.05$). Women in the highest MFS tertile, but not men, had a lower prevalence of MetS.

Adjusted odds ratios (ORs) for MetS prevalence in the low, middle, and high MFS groups, after adjusting for age, were 1.0 (referent), 0.92 (95% confidence interval [CI]: 0.51 - 1.63), and 0.53 (95% CI, 0.28 - 0.99) (P for trend = 0.04) in women; in men, they were 1.0 (referent), 0.48 (95% CI, 0.23 - 1.01), and 0.42 (95% CI, 0.19 - 0.90) (P for trend = 0.02), respectively (**Figure 1**, Model 1). In addition, after further adjusting for smoking status, alcohol intake, and exercise habits, adjusted ORs were 1.0 (referent), 0.90 (95% CI, 0.50 - 1.62), and 0.49 (95% CI, 0.25 - 0.94) (P for trend = 0.03) in women; in men, they were 1.0 (referent), 0.49 (95% CI, 0.23 - 1.04), and 0.42 (95% CI, 0.18 - 0.97) (P for trend = 0.04), respectively (**Figure 1**, Model 2).

Table 2 shows age-adjusted and multivariate-adjusted

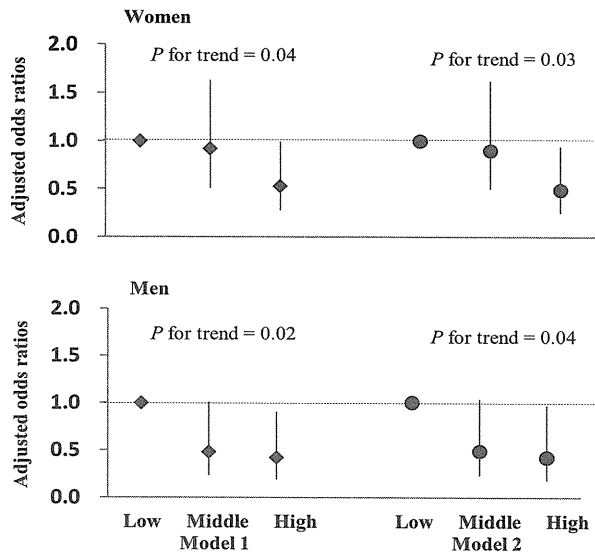


Figure 1. Adjusted odds ratios (ORs) for MetS prevalence in the low, middle, and high muscular fitness composite score (MFS) groups. Results are adjusted for age (Model 1), and additionally adjusted for smoking status, alcohol intake, and exercise habits (Model 2). Vertical bars indicate 95% CIs. Low: Low MFS; Middle: Middle MFS; High: High MFS.

ORs. In women, MFS was inversely associated with HDL-c and WC. Age-adjusted ORs for the highest versus lowest tertiles were 0.17 (95% CI, 0.05 - 0.60; *P* for trend < 0.01) for HDL-c and 0.18 (95% CI, 0.10 - 0.32; *P* for trend < 0.001) for WC; multivariate-adjusted ORs for the highest versus lowest tertiles were 0.15 (95% CI, 0.04 - 0.55; *P* for trend < 0.01) for HDL-c and 0.17 (95% CI, 0.09 - 0.32; *P* for trend < 0.001) for WC. In men, MFS was inversely associated with TG and WC: age-adjusted ORs for the highest versus lowest tertiles were 0.39 (95% CI, 0.19 - 0.79; *P* for trend < 0.01) for TG and 0.06 (95% CI, 0.02 - 0.22; *P* for trend < 0.001) for WC. However, the MFS-TG relationship was attenuated after further adjustment for smoking status, alcohol intake, and exercise habits; multivariate-adjusted ORs for the highest versus lowest tertiles were 0.54 (95% CI, 0.25 - 1.14; *P* for trend < 0.09) for TG and 0.07 (95% CI, 0.02 - 0.25; *P* for trend < 0.001) for WC.

4. DISCUSSION

In this cross-sectional study, we examined the association between MFS levels and the prevalence of MetS and

Table 2. Adjusted odds ratios (95% CIs) for MetS risk factors across MFS tertiles.

	Women (n = 335)					
	Low (n = 111)	Middle (n = 112)		High (n = 112)		<i>P</i> for trend
		ORs	95%CI	ORs	95%CI	
BP						
Model 1	1.00	0.98	(0.57 - 1.67)	0.61	(0.36 - 1.05)	0.07
Model 2	1.00	0.94	(0.54 - 1.62)	0.58	(0.33 - 1.02)	0.06
HDL-c						
Model 1	1.00	0.85	(0.38 - 1.90)	0.17	(0.05 - 0.60)	<0.01
Model 2	1.00	0.84	(0.37 - 1.88)	0.15	(0.04 - 0.55)	<0.01
TG						
Model 1	1.00	1.26	(0.72 - 2.20)	0.86	(0.48 - 1.54)	0.60
Model 2	1.00	1.30	(0.74 - 2.30)	0.87	(0.48 - 1.59)	0.62
FPG						
Model 1	1.00	0.46	(0.24 - 0.87)	0.62	(0.33 - 1.15)	0.10
Model 2	1.00	0.44	(0.23 - 0.84)	0.56	(0.30 - 1.06)	0.06
WC						
Model 1	1.00	0.38	(0.21 - 0.68)	0.18	(0.10 - 0.32)	<0.001
Model 2	1.00	0.37	(0.21 - 0.68)	0.17	(0.09 - 0.32)	<0.001
		Men (n = 209)				
	Low (n = 69)	Middle (n = 70)		High (n = 70)		<i>P</i> for trend
		ORs	95%CI	ORs	95%CI	
BP						
Model 1	1.00	1.50	(0.74 - 3.04)	1.16	(0.57 - 2.33)	0.68
Model 2	1.00	1.28	(0.62 - 2.65)	0.84	(0.39 - 1.81)	0.70
HDL-c						
Model 1	1.00	0.98	(0.27 - 3.57)	0.98	(0.26 - 3.64)	0.98
Model 2	1.00	1.27	(0.33 - 4.87)	0.90	(0.21 - 3.79)	0.80
TG						
Model 1	1.00	0.27	(0.13 - 0.54)	0.39	(0.19 - 0.79)	0.01
Model 2	1.00	0.30	(0.15 - 0.62)	0.54	(0.25 - 1.14)	0.09
FPG						
Model 1	1.00	0.36	(0.18 - 0.74)	0.68	(0.34 - 1.34)	0.24
Model 2	1.00	0.36	(0.17 - 0.74)	0.73	(0.35 - 1.54)	0.38
WC						
Model 1	1.00	0.69	(0.34 - 1.43)	0.06	(0.02 - 0.22)	<0.001
Model 2	1.00	0.72	(0.34 - 1.51)	0.07	(0.02 - 0.25)	<0.001

Model 1 is adjusted for age; Model 2 is adjusted for age, smoking status, alcohol intake, and exercise habits; BP: blood pressure; HDL-c: high-density lipoprotein cholesterol; TG: triglyceride; FPG: fasting plasma glucose; WC: waist circumference.

MetS risk factors in Japanese women and men. The primary findings of this study were that 1) low MFS levels were associated with greater risk of incident MetS in women and men, and 2) low MFS levels were associated with higher prevalence of several MetS risk factors after adjustment for age, smoking status, alcohol intake, and exercise habits.

The inverse association between muscle strength and the prevalence of MetS found in the present study is consistent with the results of previous investigations [12-14]. Jurca *et al.* reported this association in adult men using a study of cross-sectional design. They found that muscle strength (measured by one repetition maximal leg press and bench press) was associated with a significantly lower risk of developing MetS in men [12]. Further longitudinal analyses in adult men obtained comparable results [13]. In addition, Atlantis *et al.* reported an inverse association between muscle strength (handgrip strength per lean mass of the arm) and the prevalence of MetS in men [14]. The present study has extended the previous results by revealing inverse associations between MFS and the prevalence of MetS in both women and men.

By contrast, other previous studies have reported a relationship between muscle strength and MetS risk factors [15,22]. Wijndaele *et al.* reported that muscular strength assessed by measuring isometric knee extension and flexion peak torque was associated with the MetS risk factors of TG, HDL-c, and clustered MetS risk factors in women, and associated with clustered MetS risk factors in men [15]. Aoyama *et al.* examined the relationship between grip strength and individual and clustered MetS risk factors in Japanese men and women and found that grip strength was inversely associated with plasma glucose levels and clustered MetS risk factors in women [18]. Similar to previous studies, MFS was also associated with lipid profiles and WC in this study.

Although their results are not directly comparable with ours, Katzmarzyk *et al.* found a significant inverse relationship between musculoskeletal fitness composite score (calculated from the scores for sit-ups, push-ups, grip strength, and trunk flexibility) and all-cause mortality [22] and the incidence of type 2 diabetes among a Canadian population [23]. In addition, Sawada *et al.* observed a significant inverse relationship between muscular and performance fitness index composite scores (summed Z scores of sit-ups, side step, and functional reach) and the incidence of type 2 diabetes in Japanese men [24]. In their previous study, a significant inverse relationship was observed between muscular fitness and all-cause mortality and type 2 diabetes. These results suggest that maintaining a high level of MFS may prevent the development of MetS and reduce the risk of type 2 diabetes and mortality.

Strength training may lower MetS risk, including improvement in TG and HDL-c [25], BP [26], central adiposity and body composition [27], and whole-body insulin action and glucose uptake [28,29]. The metabolic effects of reduced muscle mass secondary to aging, decreased physical activity, or both contribute to the presence of obesity, insulin resistance, type 2 diabetes, dyslipidemia, and hypertension [30]. Skeletal muscle, the primary tissue for glucose and triglyceride metabolism, is a determinant of resting metabolic rate, and changes in muscle mass may reduce multiple CVD risk factors [31]. Therefore, with the maintenance of high muscle strength, such as that achieved by resistance training, may prove effective for the prevention and treatment of MetS.

This study has some limitations. First, the causality of relationships cannot be determined due to its cross-sectional design. Longitudinal or interventional studies are required to demonstrate this association further. Second, our sample size is small. In order to better clarify these relationships, future research should be done to increase the sample size.

In conclusion, this study suggests that muscular fitness is inversely associated with MetS in Japanese women and men aged 30 - 79 y. This finding may indicate a protective effect of muscular fitness on MetS. Furthermore, muscle fitness was associated with a better profile for several risk factors of MetS.

5. ACKNOWLEDGEMENTS

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