表2　サルコペニア選定に用いた骨格筋量のカットポイント

報告者	筋量の測定法	定　義	男　性	女　性
Baumgartner, et al	DEXA	ASM/Ht^2, 若年成人2SD↓	7.26	5.45
Tanko, et al	DEXA	ASM/Ht^2, 若年成人2SD↓	*	5.40
Janssen, et al	BI	SMI	8.50	5.75
Chien, et al	BI	SMI, 若年成人2SD↓	8.87	6.42
Sanada, et al	DEXA	ASM/Ht^2, 若年成人2SD↓	6.87	5.46

ASM (kg) = appendicular skeletal muscle mass estimated by DXA.
SM (kg) = skeletal muscle mass estimated by BI.
SMI = SM/Ht^2, Ht = height.
（文献4より引用）

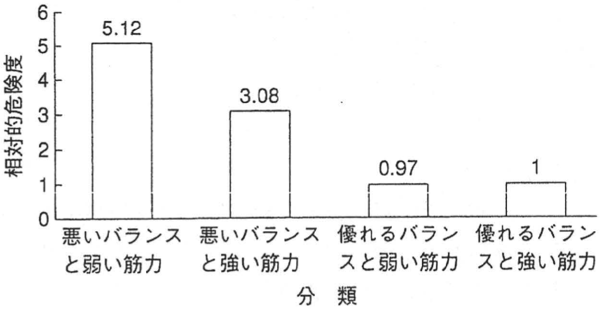

図1　歩行障害の予知因子
（文献5より引用）

提案するとともに，disabilityと密接に関連する（表2）ことから，サルコペニアは高齢期の大きな健康問題としてとらえるべきであると強調している[4]．

歩行機能には筋力とバランスが密接に関わっている

歩行機能は，体力全般の代表的な指標である．外出を楽にし，活動範囲を広げ，元気で長生きを実現するためには，歩行機能の維持・向上は不可欠な要素である．高齢者歩行パターンの特徴は，歩行速度の低下，歩幅の短縮，歩隔の増大，両脚支持時間の延長，遊脚期での足の挙上の低下，腕の振りの減少，不安定な方向転換などである．高齢者に多くみられる歩行機能の低下は，死亡率の上昇，転倒率の増加，生活機能の障害など，様々な指標と密接に関わっていることが多くの研究で指摘されている．

Rantanenらが，65歳以上の高齢女性758名を対象に3年間追跡調査し，歩行障害の発生と関連する要因について検討した結果によれば，「筋力の減少とバランス能力の低下」という条件の対象者は「優れる筋力とバランス機能」を有する対象者に比べて，歩行障害発生の危険性の高いことを指摘し（RR＝5.12，95% CI＝2.68–9.80），歩行機能を維持するためには筋力向上とバランス機能の改善が必要であると強調している（図1）[5]．

サルコペニアの高齢者の特徴

筆者は，大都市部在住の75歳以上の後期高齢女性1,399名を対象に，「四肢の骨格筋量が少ない」「BMIが低い」「膝伸展力が低い」3つの基準に該当する場合をサルコペニアと定義し，該当者304名（21.7%）を抽出し，特徴を調べている．その結果によれば，サルコペニア高齢者は，年齢が高く，下腿三頭筋周囲，BMI，筋肉量は低値を示すとともに健康度自己評価，定期的な運動習慣をもっている者の割合も低いという傾向である．しかし，外出頻度が少ない者の割合は高値を示し，サルコペニアと判定された高齢者は活動量が少なく，自分の健康に対する自信感を喪失している者が多いと推測できる．一方，既往歴においては，貧血症，骨粗鬆症，骨折歴は有意に高い割合を示しているが，高血圧症，脂質異常症は正常群より低い割合を示していることから，サルコペニア高齢者の場合，骨粗鬆症に伴う骨折危険性が高いことが示唆されている（表3）．さらに，サルコペニア高齢者の歩行機能を調べるために，5mの最大歩行速度を計測し，サルコペニア群と正常群を比較したところ，図2に示した通りに，サルコペニア群は1.58±0.34 m/sec，正常群は1.71±0.36 m/secとして，サルコペニア群の歩行速度が有意に低いことが確認されている[6]．

サルコペニアと関連する要因

老化に伴う筋骨格筋量減少の原因としては，加齢，IGF-1の分泌減少，慢性疾患，アンドロゲン・エストロゲン分泌の減少，炎症性サイトカインの増加，身体活

表3　サルコペニア群と正常群の調査項目の比較

項目	サルコペニア群	正常群	p値
年齢(歳)	79.49±2.93	78.51±2.77	<0.001
下腿三頭筋周囲(cm)	30.17±2.03	33.92±2.60	<0.001
BMI(kg/m^2)	18.98±2.01	23.74±2.84	<0.001
筋肉量(kg)	26.92±2.61	31.73±3.16	<0.001
健康度自己評価，健康(%)	75.7	85.8	<0.001
外出頻度，少ない(%)	4.6	2.5	0.051
運動習慣，有(%)	27.3	33.5	0.039
既往歴，有(%)			
高血圧	51.0	58.0	0.029
高脂血症	32.2	40.5	0.009
貧血症	4.6	2.2	0.022
骨粗鬆症	38.2	30.7	0.014
骨　折	28.6	22.9	0.038

（文献6より引用）

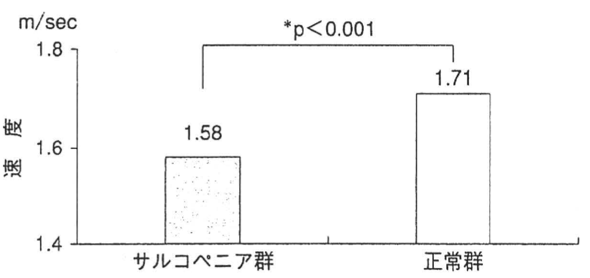

図2　サルコペニア判定者と通常者の最大歩行速度の比較
（文献6より引用）

動量の減少，栄養摂取量の不足が指摘されているが，そのメカニズムは未だ完全には解明されていない．しかし，これらの要因が複合的に作用した結果，筋タンパク質の分解量が合成量を上回ることによって，骨格筋量は徐々に減少するのである．しかし，骨格筋タンパク質合成を促進することができれば，筋量の減少を抑制し，有効なサルコペニア対策として考えられる．

高齢者においても，レジスタンス運動によって，筋肉量や筋力の増大効果が確認されている[7]．さらに，必須アミノ酸の投与によって骨格筋タンパク質の合成促進も認められている[8]ことから，運動と必須アミノ酸補充は有効なサルコペニア対策として注目されている．

サルコペニア改善のための運動，アミノ酸補充の効果

地域在住サルコペニア高齢者の筋力向上や歩行機能の改善には，どのような取り組みが有効であるかに対する答えを得るために行った介入について，簡単に紹介する．

介入効果を確実に得るためには，サルコペニアと関連する様々な要因の中で，可変因子を見出すことが必要である．筆者は，サルコペニアには不活動と筋タンパク質合成能力の低下が密接に関わっているとの先行研究に着目し，不活動を解消するための運動指導，筋タンパク質の合成を促進するための必須アミノ酸補充の効果について調べている．

介入効果を客観的に検証するために，介入参加希望者をRCTにより運動群と栄養群に分け，運動群には週2回，1回当たり60分間の筋力強化と歩行機能の改善を目的とした包括的運動指導を，栄養群にはロイシン高配合のアミノ酸3gを1日2回補充する指導を，3カ月間実施した．介入前後における身体組成，体力，老年症候群の改善の度合いを検討した．その結果，LBMは運動群で2.4%，栄養群で4.6%の有意な向上が，歩行速度は，運動群で18.6%，栄養群で10.3%の顕著な向上が確認され(図3)，地域在住サルコペニア高齢者の身体組成や体力を改善するためには，運動指導のみならずアミノ酸補充も有効であることが示唆されている．しかし，サルコペニア高齢者に多く観察される尿失禁は，運動群で38.9%から19.4%(P=0.021)と有意に改善されたが，栄養群では有意な改善が認められてない．以上のことから，サルコペニア高齢者のLBMあるいは体力の改善を目的とした場合には，運動指導のみならず栄養補充も有効な手法であることが確認されたが，サルコペニア高齢者に有症率の高い老年症候群の改善には，運動介入の効果が優れる可能性が示唆されている．

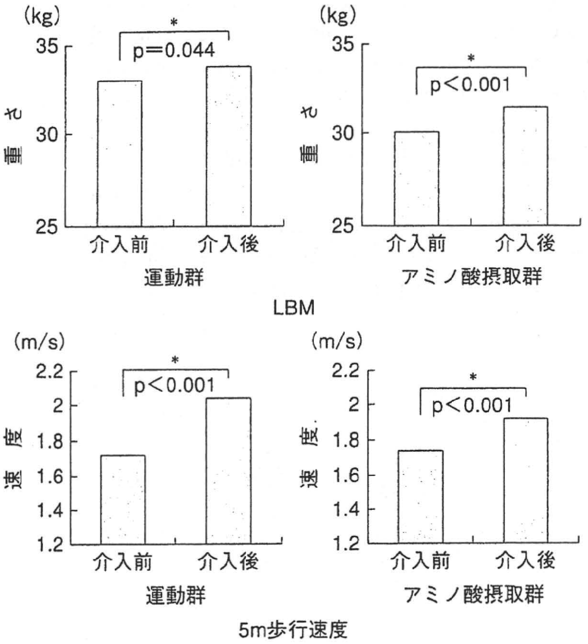

図3　3カ月間の運動，アミノ酸摂取の介入がLBMおよび歩行速度に及ぼす影響

（文献9より引用）

骨格筋量の減少や筋力の衰えと定義されるサルコペニアの改善に効果的な取り組みは，ロコモの改善にも応用できると考えられる．なぜならば，筋力の低下はロコモティブシンドローム出現と強く関わっているからである．

おわりに

骨格筋量の減少に伴う筋力の衰えを意味するサルコペニアは後期高齢者において有症率が上昇し，身体機能の障害や死亡と強く関連していることが指摘されている．サルコペニアと関連する要因は様々で複雑であるが，不活動や栄養など可変要因の改善に焦点を当てた改善策の効果を検討したところ，骨格筋量の増加，体力の向上には，運動指導，栄養指導ともに有効であった．しかし，サルコペニア高齢者に多くみられる老年症候群の解消には，運動指導がより有効であることを検証した．

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The Relationship between Sarcopenia and Locomotive Syndrome in Elderly People

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The prevalence of sarcopenia, which is the loss of skeletal muscle mass and muscle strength, has increased among the elderly and it has been indicated that sarcopenia is strongly related to functional disability, falls, morbidity, and mortality. Locomotive syndrome is a musculoskeletal disorder which decreases mobility and increases the risk of admission to long-term care. Physical activity

is the result of the combination of structures and organs such as bones, muscles, joints and nerves functioning together, and smooth movement is difficult when one of these structures disorder. Here we have assumed that the potentially preventable factor relating locomotion and sarcopenia is the decrease in muscle strength, and we have also described effective interventions to improve walking ability.

Although there are many complex factors related to locomotion and sarcopenia, but we have focused on the examination of reversible factors such as inactivity and nutrition. As a result, guidance and direction in both exercise and nutrition supplementation were effective in increasing skeletal muscle mass and muscle strength. However, exercise was more effective in reducing geriatric syndrome such as urinarg incontinence often seen in sarcopenic older adults.

Archives of Gerontology and Geriatrics 52 (2011) 99–105

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

The effects of multidimensional exercise on functional decline, urinary incontinence, and fear of falling in community-dwelling elderly women with multiple symptoms of geriatric syndrome: A randomized controlled and 6-month follow-up trial

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ARTICLE INFO

Article history:
Received 6 April 2009
Received in revised form 12 December 2009
Accepted 5 February 2010
Available online 7 March 2010

Keywords:
Functional decline
Urinary incontinence
Fear of falling
Multiple symptoms of geriatric syndrome
Multidimensional exercise

ABSTRACT

This study assessed the effects of multidimensional exercises on functional decline, urinary incontinence, and fear of falling in community-dwelling Japanese elderly women with multiple symptoms of geriatric syndrome (MSGS). Sixty-one participants were randomly assigned either to an intervention ($n = 31$) or to a control group ($n = 30$). For 3-month period, the intervention group received multidimensional exercise, twice a week, aiming to increase the muscle strength, walking ability, and pelvic floor muscle (PFM). Outcome variables were measured at baseline, and after intervention and follow-up. The functional decline of the intervention group decreased from 50.0% at baseline to 16.7% after intervention and follow-up ($Q = 16.67$, $p < 0.001$). For urinary incontinence, the intervention group decreased from 66.7% at baseline to 23.3% after intervention and 40.0% at follow-up ($Q = 13.56$, $p = 0.001$), whereas the control group showed no improvement. Intervention group showed greater and significant decrease in the score of MSGS compared to control group ($F = 12.66$, $p = 0.001$). Within the subjects that showed improvement to normal status of MSGS, a significantly higher proportion demonstrated increased maximum walking speed at follow-up ($Q = 6.50$, $p = 0.039$). These results suggest that multidimensional exercise is an effective strategy for reducing geriatric syndromes in elderly population. An increase in walking ability may contribute to the improvement of MSGS.

1. Introduction

The geriatric syndrome such as functional decline, urinary incontinence, and fear of falling are used to capture those clinical conditions that do not fit into discrete disease categories, and are serious problems among the elderly population (Inouye et al., 2007). Many studies have demonstrated that a decline in walking speed, muscle strength and balance ability of the elderly is strongly associated with the development of geriatric syndrome (Vellas et al., 1997; Ishizaki et al., 2000; Maggi et al., 2001).

It is well documented that as age advances, the proportion of people with more than one symptom of geriatric syndrome increases. In addition, people with MSGS have an increased prevalence of functional disability and mortality compared to people with only one or no symptoms present. Several studies have put emphasis on the fact that multidimensional exercises focusing on strength, balance, and mobility improvement, even into advanced age, was helpful in reducing functional decline, urinary incontinence and fear of falling (Nelson et al., 2004; Gitlin et al., 2006; Kim et al., 2007). These previous studies validated the effectiveness of the multidimensional exercises focusing on the improvement of a single geriatric syndrome such as functional decline or urinary incontinence, but did not provide any information on whether the subjects possessed symptoms other than functional decline or urinary incontinence. One study demonstrated (Tinetti et al., 1995) that falls and urinary incontinence were associated with the occurrence of functional decline, and that the identification of shared risk factors associated with falls and urinary incontinence is the key in establishing effective and efficient interventional strategies. However, few multidimensional exercises studies have been performed in community-dwelling elderly persons with MSGS.

In the present study, we hypothesize that deteriorations in muscle strength, walking and balance ability are common risk factors associated with functional decline, urinary incontinence and fear of falling. We conducted a randomized and controlled trial to evaluate the effects of the multidimensional exercises targeted at reducing the symptoms of functional decline, urinary inconti-

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doi:10.1016/j.archger.2010.02.008

nence, and fear of falling in community-dwelling Japanese elderly women with MSGS.

2. Methods

2.1. Study sample and procedures

Overall health surveys were conducted at the Tokyo Metropolitan Institute of Gerontology (TMIG), aiming at early screening of geriatric syndromes in elderly persons and at developing intervention strategies, which would reduce those geriatric syndromes. As subjects, 1016 women were chosen randomly from the Basic Resident Register as persons aged 70 or older residing in Itabashi ward of Metropolitan Tokyo.

A letter outlining the study and describing its objective, and the way that the personal data would be used was mailed to the elderly women selected, inviting them to participate in the study. The baseline survey was conducted in November 2004, and 669 women aged 70 years and older participated.

The participants were screened based on three geriatric syndromes: functional decline, urinary incontinence, and fear of falling. A person who was reported as having two or more geriatric syndromes present was defined as having MSGS. Out of the 669 women participated, 102 were classified as having MSGS (Fig. 1). A pamphlet containing information on the "Exercise Classes for the Treatment of Geriatric Syndromes" was mailed to the 102 potential participants. A response was obtained from 74 of them, of whom 61 were willing to participate. There were no statistically significant differences in physical fitness, age, and geriatric syndromes between the 61 willing participants and the 41 unwilling ones including those who did not submit any response. The research protocol was approved by the institutional review board, and informed consent was obtained from each participant.

2.2. Randomization

After baseline assessment, subjects were divided into two groups with an allocation ratio of 1:1 according to computer-generated random numbers. There was no attempt to equalize the sizes of the groups based on characteristics or to recruit subjects with specific characteristics. Thereafter, one group was allocated to the intervention ($n = 31$) and the other group to the control ($n = 30$) (Fig. 1).

2.3. Data collection

Data collected by interview and a physical fitness test at baseline, after 3-month exercise, and were reassessed at 6-month follow-up.

2.3.1. Interview survey

A face-to-face interview was conducted to assess the following variables: The functional decline was measured using the TMIG index of competence (Koyano et al., 1991). For each of the 13 items, "yes" was scored as 1 and "no" as 0 (maximum score: 13). A person with a TMIG index score less than 10 was defined as having functional decline. Urinary incontinence was assessed through the question "Have you ever experienced urine leakage during the last 1 year?" If a subject responded with a "yes", we would then ask concerning the frequency of urinary incontinence. The frequency of urinary incontinence was assessed based on a five-point scale through interview (1: several times per year; 2: once or more per month: 3: once or twice per week; 4: once every 2 days; 5: everyday). A person whose response ranged 2–5 was defined as having urinary incontinence (Burgio et al., 1991). The fear of falling was assessed by asking "At this moment, are you afraid of falling?" and classified as "1. not at all", "2. somewhat", "3. very much", and "4. activity restriction due to fear of falling". Subjects who responded within 2 and 4 were assigned to the fear group (Maki et al., 1991).

The effect of the multidimensional exercises on the geriatric syndromes was assessed based on shifts of the responses from the interview, which was conducted at a baseline, completion of the 3-month exercise, and at the 6-month follow-up. The scores of geriatric syndromes were calculated as follows: functional decline, 0 for TMIG index score more than 11, 1 for 10, 2 for 9, and 3 for less than 8; urinary incontinence, 0 for no urine leakage or several times per year, 1 for once or more per month, 2 for once or twice per week, and 3 for once every 2 days or everyday; fear of falling, 0 for not at all, 1 for somewhat, 2 for very much, and 3 for activity restriction due to afraid of falling. The score of MSGS was calculated as add up three geriatric syndrome score (functional decline, urinary incontinence, and fear of falling). And, a participant with a MSGS score less than 1 was defined as improvement of MSGS.

2.3.2. Physical fitness test

Body mass index (BMI) was calculated from body weight (kg) divided by height (m) squared. Physical fitness tests were used for the assessment of muscle strength, walking speed, and balance ability. The following standardized tests were performed: grip strength (Suzuki et al., 2004); adductor muscle strength (Kim et al., 2007); usual and maximum walking speed (Suzuki et al., 2004); one leg standing time with eyes open (Suzuki et al., 2004); tandem walking (Speers et al., 1998); functional reach (Duncan et al., 1990). The staff members who performed the assessments did not know the subjects' group assignments.

2.4. Interventions

2.4.1. Exercise group

The exercise group participated in an intervention comprised of 60-min exercise sessions held at the TMIG Health Promotion Classes, twice per week for 3-month. Weight-bearing exercise: strength training of the thigh, abdominal, and back muscles was performed and included bending the knees, and other similar exercises.

PFM exercise: The exercise regimen was designed to strengthen the fast- and slow-twitch muscle fibers located at the pelvic floor. Participants were initially instructed to perform 10 fast contractions (3-s) with a 5-s relaxation period and 10 sustained contractions (6–8 s) with a 10-s relaxation period in between the contractions. The PFM exercise was performed in sitting, lying, and standing positions with legs apart, emphasizing training of the PFM and relaxation of the other muscles.

Chair exercises: Used in the early stage of the program. The exercises included seated toe and heel raises, seated lift foot and point/flex toes, and others.

Resistance band exercise: Focused on increasing the strength of the muscles of the upper extremities, abdomen, and lower extremities in frail elderly people (arm pull back, leg extension, and others).

Ball exercise: Exercises with a training ball were conducted using a small (diameter: 21 cm) and a large ball (diameter: 45–55 cm), aiming to increment the muscle strength and balance (sitting on the ball and extending legs, and others).

Walking ability training: Focused on maintenance of stability during walking and on the improvement of responses to postural changes during walking (walking with directional changes, gait pattern variations and enhancement, and others).

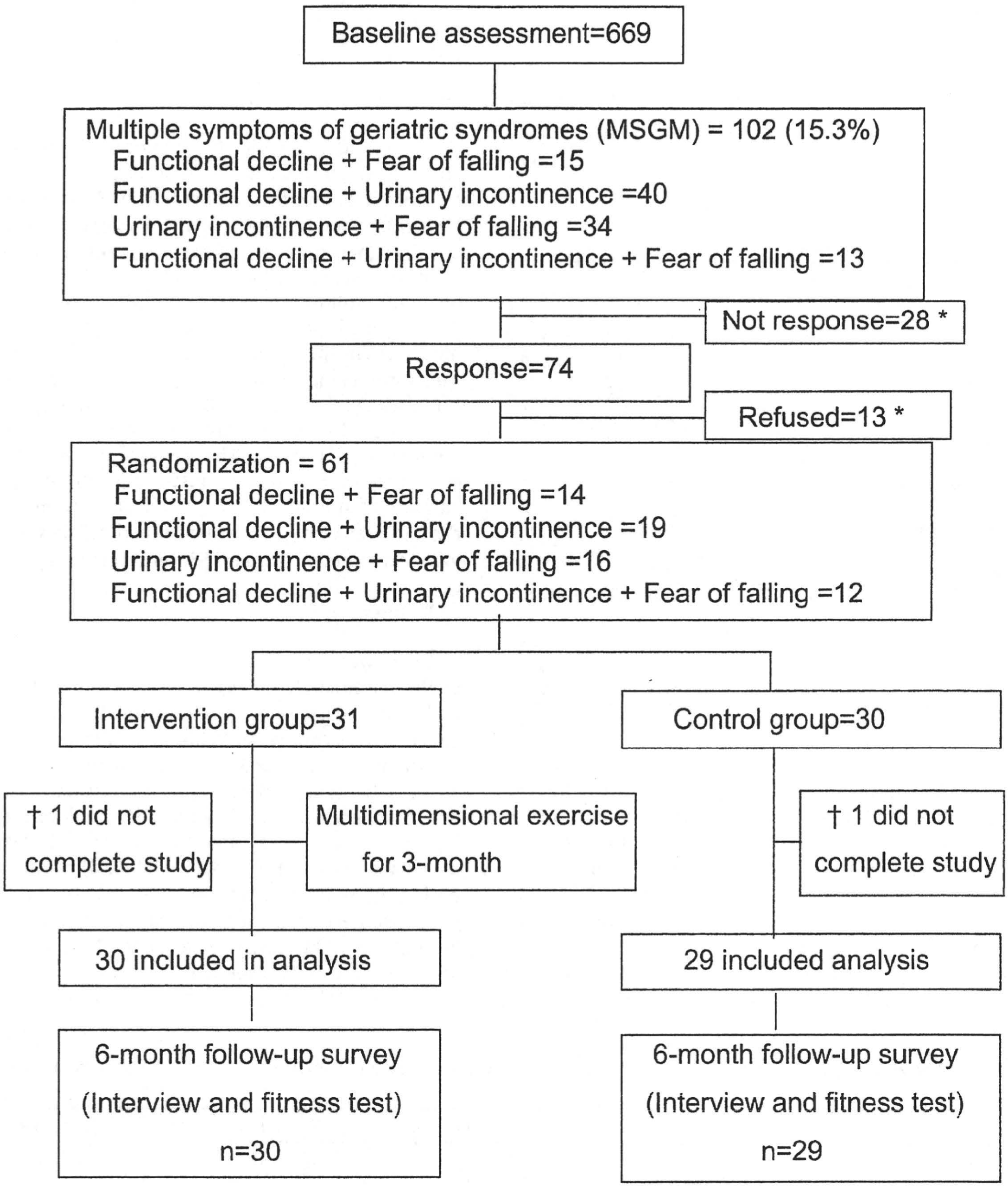

Fig. 1. Flow chart of participants through the randomized controlled trial of the exercise program and analysis. (*) Forty-one of MSGM ($n = 102$) were excluded due to the not response ($n = 28$) and refusal ($n = 13$). (†) Two subjects could not complete the study because of hospitalization ($n = 1$), and fracture ($n = 1$).

Balance training: Focused on the improvement of the static, dynamic, and lateral balancing ability (multidirectional weight shifts, tandem walking, and others).

2.4.2. Control group

The control group attended a general health education class (albumin, osteoporosis, and prevention of malnutrition) held at the TMIG once a month for a 3-month period.

2.5. Follow-up and compliance

During the 6-month follow-up period, subjects of the intervention group attended group exercise classes (60 min) once per month in addition to receiving a home-based exercise program. The home-based exercise program consisted of two to three sets of the 15 exercises and PFM exercise that they had learned during the group exercise session. They were also advised to do the home-based exercises at least three times or more per week for about 30-min per day. In order to accurately monitor the exercise times and the number of sets performed at home during the follow-up period, a pamphlet illustrating the PFM and strengthening exercises and a recording sheet were distributed to the participants, who were instructed to record the time and sets of exercises performed at home everyday. The record sheets were collected once a month at the group exercise class and analyzed in order to calculate the mean exercise frequency per week, and the mean exercise time per day.

2.6. Statistical analysis

Both the mean and standard deviation were calculated for each variable. The differences in the baseline data between the

Table 1
Selected variable characteristics of participants at baseline by study group, mean ± S.D.

Variables	Intervention group	Control group	$p^{\dagger}$
Number	31	30	
Age (year)	79.0 ± 3.9	78.1 ± 4.4	0.424
Height (cm)	146.9 ± 5.4	147.0 ± 5.8	0.940
Body weight (kg)	47.4 ± 6.4	50.7 ± 9.1	0.108
BMI (kg/m^2)	22.0 ± 2.6	23.4 ± 3.6	0.084
One leg standing time (s)	29.2 ± 23.5	34.6 ± 22.8	0.367
Tandem walking (step)	7.2 ± 4.7	7.8 ± 4.7	0.631
Functional reach (cm)	31.0 ± 7.1	33.2 ± 4.9	0.167
Grip strength (kg)	16.5 ± 4.3	17.9 ± 4.7	0.239
Adductor muscle strength (kg)	17.3 ± 4.0	18.0 ± 5.1	0.740
Usual walking speed (m/s)	1.1 ± 0.3	1.2 ± 0.2	0.685
Maximal walking speed (m/s)	1.7 ± 0.4	1.7 ± 0.4	0.979
TMIG index score (point)	10.6 ± 1.6	10.4 ± 1.5	0.654
Urinary incontinence, yes (%)	64.5	50.0	0.252
Functional decline, yes (%)	51.6	43.3	0.517
Fear of falling, yes (%)	67.7	76.7	0.390
Chronic medical conditions, yes (%)			
Hypertension	58.1	60.0	0.902
Stroke	13.2	13.3	0.988
Diabetes	19.4	20.0	0.948

† Two group *t*-test for continuous variables and the χ^2-test for categorical variables.

exercise and control group were analyzed using *t*-test for the continuous variables and Chi-square test for the categorical variables. The changes in dependent variables pre-intervention, post-intervention and follow-up in the exercise and control group were analyzed using an analysis of variance (ANOVA) with repeated measures. Significant interactions were analyzed to determine whether or not the effects were greater in the intervention than the control group. Cochran's *Q*-test was used to evaluate within-group differences of the effect of the exercise on the categorical variables for pre-intervention, post-intervention, and follow-up data. In the case of items which were showing significant differences, a post hoc analysis was performed using McNumar's test. One-way ANOVA was performed to evaluate the within-subgroup effect of the intervention on multiple geriatric syndrome scores at baseline, after the 3-month exercise, and at 6-month follow-up. For the subgroup showing significant differences, a post hoc analysis was performed using Scheffe's method. The percentage improvement in physical fitness was calculated using the following formula: % improvement = {(after 3-month exercise or at 6-month follow-up values − baseline value)/baseline value × 100}. The percentage improvement was divided into tertiles. The power of the current study was calculated at 80% to demonstrate a difference in the outcome variable of at least 20% at a significance level of alpha = 0.05. All the analyses were performed using the SPSS software package for Windows version 15.0 (SPSS, Inc., Tokyo, Japan).

3. Results

There were no significant differences between the groups in any of the baseline characteristics such as age, BMI, walking speed, adductor muscle strength, functional decline, urinary incontinence, fear of falling, and chronic medical conditions (Table 1).

Attendance 15 (62.5%) or more than of the exercise sessions (24) was defined as trial completion. Two participants (3.3%) could not complete the trial after the randomization because of hospitalization (n = 1) and fracture (n = 1) (Fig. 1). The mean attendance rate was 77.4% (61.3–90.3%) during the intervention period and 74.2% during the follow-up. In the exercise group, 32.3% of the subjects attended the exercise sessions 24 times, 22.6% attended 20–23 times, 35.5% attended 16–19 times, 6.5% attended 15 times, and 3.3% attended 14 or less of the exercise sessions. During the follow-up, the mean frequency of performing the

Table 2
Comparison of physical fitness and geriatric syndrome variables between intervention = I (n = 30) and control = C (n = 29) groups after 3-month exercise and at 6-month follow-up, mean ± S.D.

Variables	Gr	Baseline	3-Month exercise	6-Month follow-up	ANOVA F=	p=
Body weight (kg)	I	46.6 ± 5.4	47.4 ± 5.4	47.1 ± 5.4	(1,57) = 2.74	0.105
	C	51.0 ± 9.5	51.0 ± 9.4	50.6 ± 9.1		
BMI (kg/m^2)	I	21.5 ± 2.2	21.9 ± 2.2	21.8 ± 2.2	(1,57) = 2.82	0.100
	C	23.4 ± 3.9	23.4 ± 3.8	23.3 ± 3.6		
One leg standing time (s)	I	34.0 ± 24.2	28.2 ± 20.4	32.4 ± 22.6	(1,57) = 0.01	0.920
	C	33.4 ± 23.4	28.8 ± 23.5	32.4 ± 24.6		
Tandem walking (step)	I	7.2 ± 4.7	6.1 ± 4.5	5.9 ± 3.3	(1,57) = 4.70	0.036
	C	7.8 ± 4.7	5.2 ± 3.8	3.5 ± 2.0		
Functional reach (cm)	I	31.7 ± 6.8	33.5 ± 5.13	3.5 ± 4.4	(1,56) = 4.18	0.046
	C	33.7 ± 4.7	32.7 ± 5.3	31.6 ± 8.8		
Grip strength (kg)	I	17.2 ± 4.0	20.9 ± 5.2	17.9 ± 4.7	(1,57) = 0.02	0.874
	C	18.0 ± 4.6	21.5 ± 5.1	18.6 ± 4.8		
Adductor muscle strength (kg)	I	17.2 ± 4.0	18.9 ± 5.1	19.3 ± 4.7	(1,57) = 4.18	0.045
	C	17.9 ± 5.0	18.2 ± 4.01	17.8 ± 3.7		
Usual walking speed (m/s)	I	1.1 ± 0.3	1.1 ± 0.2	1.2 ± 0.2	(1,57) = 13.03	0.001
	C	1.2 ± 0.2	1.1 ± 0.3	1.1 ± 0.3		
Maximal walking speed (m/s)	I	1.7 ± 0.4	1.8 ± 0.5	1.8 ± 0.4	(1,56) = 4.24	0.044
	C	1.7 ± 0.4	1.6 ± 0.4	1.6 ± 0.4		
Functional decline, yes (%)	I	50.0	16.7	16.7	16.67[a]	<0.001
	C	41.4	31.0	27.6	4.10[a]	0.109
Urinary incontinence, yes (%)	I	66.7	23.3	40.0	13.56[a]	0.001
	C	51.7	44.8	44.8	4.00[a]	0.135
Fear of falling, yes (%)	I	66.7	70.0	70.0	0.17[a]	0.920
	C	75.9	62.1	75.9	2.91[a]	0.234

[a] Cochran's *Q*-value.

Table 3
Improvement of MSGS according to maximum walking speed and adductor muscle strength tertiles in intervention group.

Survey variable	Changes compared to baseline[a]	Improvement of MSGS[†] n (%)	Cochran's Q-value	p	Post hoc[†]
3-Month exercise (n = 8)					
Maximum walking speed	Increased	3 (37.5)	2.80	0.247	
	No change	4 (50.0)			
	Decreased	1 (12.5)			
Adductor muscle strength	Increased	3 (37.5)	0.50	0.779	
	No change	3 (37.5)			
	Decreased	2 (25.0)			
6-Month follow-up (n = 7)					
Maximum walking speed	Increased	5 (71.4)	6.50	0.039	In > De
	No change	1 (14.3)			
	Decreased	1 (14.3)			
Adductor muscle strength	Increased	3 (42.8)	0.57	0.713	
	No change	2 (28.6)			
	Decreased	2 (28.6)			

[a] Decreased (De) means lower range (0.0–33.3%), no change (no) means medium range (33.4–66.6%), and increased (In) means upper range (66.7–100%) of tertile.

exercise series at home was 3.8 times per week (23.3% performed everyday, 50.0% 2-3 times per week, 26.7% once or less per week), while the mean exercise time was 29.0 min.

The exercise group showed significant improvement compared with the control group in muscle strength, walking speed and balance. There was a significant group by time interaction for tandem walking ($F = 4.70$, $p = 0.036$), functional reach ($F = 4.18$, $p = 0.046$), adductor muscle strength ($F = 4.18$, $p = 0.045$), usual walking speed ($F = 13.03$, $p = 0.001$), and maximum walking speed ($F = 4.24$, $p = 0.044$) with significantly greater increases in the exercise group. The functional decline decreased significantly from 50.0% at baseline to 16.7% after the intervention and follow-up in the exercise group ($Q = 16.67$, $p < 0.001$), whereas the changes were not significant in the control group. Urinary incontinence was decreased significantly from 66.7% at baseline to 23.3% after the intervention and to 40.0% at the follow-up ($Q = 13.56$, $p = 0.001$) in the exercise group. However, no significant changes observed in the control group. There were no significant changes concerning fear of falling in either group (Table 2).

Fig. 2 shows the changes in the scores of multiple geriatric syndromes. As shown in Fig. 2, the intervention group showed greater and significant decrease compared with the control group ($F = 12.66$, $p = 0.001$). Within-group scores were compared, and significant changes were observed in intervention group, with the score of multiple geriatric syndromes decreasing significantly after 3-month exercise and at 6-month follow-up ($F = 16.89$, $p < 0.001$).

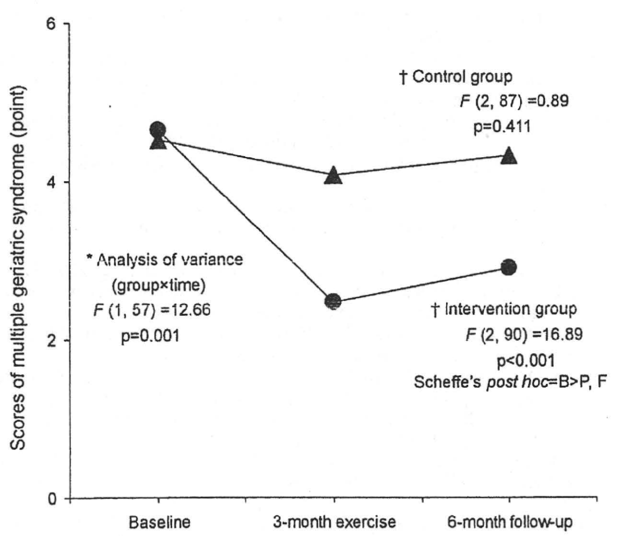

Fig. 2. Change in mean scores of MSGS at baseline, after 3-month exercise, and at 6-month follow-up in intervention (●) and control (▲) group. (*) Comparison of multiple geriatric syndrome scores between intervention and control group. (†) Comparison of within-group multiple geriatric syndrome scores at baseline (B), after the 3-month exercise (P), and at 6-month follow-up (F).

Eight subjects after 3-month intervention and seven subjects after 6-month follow-up were improved to normal status of multiple symptoms in the intervention group. Table 3 shows the distribution of the subjects who showed improvement to normal status of multiple symptoms according to the tertiles of maximum walking speed and adductor muscle strength. Within the subjects that showed improvement to normal status of multiple symptoms, a significantly higher proportion had an improved maximum walking speed at the 6-month follow-up ($Q = 6.50$, $p = 0.039$) compared with those having maintained or decreased walking speed. There was no difference at either time point in the proportion of the improved subjects with increased adductor muscle strength.

4. Discussion

This study demonstrates that the 3-month, multidimensional exercises, consisting of progressive strength training, balance and walking ability exercises along with PFM exercises, improved the usual walking speed, maximum walking speed, abductor muscle strength, tandem walking and functional reach in community-dwelling elderly women with MSGS. Furthermore, the increment of the physical fitness components appeared to contribute greatly to the improvement of the functional decline, urinary incontinence, and multiple symptoms. Therefore, the results of this study suggest that the improvements of the muscle strength, walking speed, and balance, which have been reported as risk factors for geriatric syndromes, may be effective in the improvement of geriatric syndrome.

Several studies of multidimensional intervention trials have reported beneficial effects (Tinetti et al., 1994; Shumway-Cook et al., 1997; Nelson et al., 2004; Gitlin et al., 2006; Kim et al., 2007). In a recent study, Gitlin et al. (2006) conducted a multidimensional home-based intervention in elder adults with functional difficulties, and confirmed that activity of daily living (ADL), instrumental ADL, self-efficacy, fear of falling, and home hazards were all improved and that the effects were sustained even after 6-month. Kim et al. (2007) assessed the effect of PFM and fitness exercises in improving urinary incontinence in elderly community-dwelling Japanese with stress urinary incontinence, and confirmed that decrease in BMI and increase in walking speed may contribute to the treatment of urinary incontinence.

In this study, the prevalence of the functional decline decreased significantly from 50.0% before the intervention to 16.7% after intervention and follow-up. The cure rate of urinary incontinence was 43.3% after the 3-month exercise and 26.7% at 6-month follow-up for the intervention group. On the other hand, no significant improvement was observed in the control group. The effects of this multidimensional exercise affecting only a single symptom of urinary incontinence or functional decline were consistent with previously reported studies. Although the previous studies using multidimensional intervention were targeted to treat only a single geriatric syndrome, the current study was aiming to treat MSGS. Our findings suggest that the multidimensional intervention was significantly effective in the improvement of geriatric syndrome.

We analyzed the relationship between the increment of the physical fitness components and the improvement of the multiple symptoms, despite the small sample size. We found an increment rate of 9.6% in adductor muscle strength after the 3-month exercise and a rate of 12.3% after the follow-up in the intervention group, whereas the changes were not significant for the control group. This difference in the increment rate of muscle strength is not considered to account for the difference in geriatric syndrome improvement rate. However, the proportion of the subjects with improved to normal status of multiple symptoms was significantly higher among those who demonstrated an increase in maximum walking speed at 6-month follow-up ($Q = 6.50$, $p = 0.039$). These results suggest that the increment of walking speed is a major factor for the improvement of the multiple symptoms present in this population. The increased walking ability probably allowed the subjects to increase their physical activity and consequently contributed to the improvement of their functional capacity. But, the current study's results were obtained based on a small sample size. The above relationships need to be further researched in a population study which would contain a larger number of subjects and for a longer follow-up period.

Despite the fact that many studies have reported that exercise is effective in reducing the fear of falling in the elderly (Tennstedt et al., 1998), our intervention had no effect on the fear of falling in both groups. This may be explained by the characteristics of the intervention provided in the present study. Our multidimensional exercises focused on increasing the physical function and did not provide measures such as psychological care. These findings indicate that the comprehensive strategy designed to reduce MSGS in community-dwelling elderly women should include not only exercises addressing to the improvement of the physical functions, but should also incorporate psychological care focusing on reducing the fear of falling.

This study has several limitations. Firstly, the functional decline, urinary incontinence, and fear of falling were assessed using self-reported data obtained through a face-to-face interview, and they were not confirmed by objective and clinical methods. However, several previous studies have indicated that self-reported data have high validity, reliability and objectivity in the analyses of the functional decline, urinary incontinence, and fear of falling (Smith et al., 1990; Howland et al., 1993; Resnick et al., 1994). Therefore, the use of data collected from interviews or self-recording in analyses has minor influence on the interpretation of the results of this study. Secondly, although this study indicates that improvement of physical fitness components such as muscle strength and walking ability contributes to the treatment of geriatric syndrome, it provides no explanation of the mechanism of how increasing functional fitness component improves multiple geriatric symptoms.

5. Conclusions

This study assessed the effects of multidimensional exercises on functional decline, urinary incontinence, and fear of falling in community-dwelling Japanese elderly women with MSGS. The intervention program targeted modification of physical fitness may contribute to a reduction of the functional decline and urinary incontinence, but was not a diminishing symptom over time concerning the fear of falling. Therefore, the intervention strategies designed to reduce MSGS in elderly persons should include not only exercises aiming to the improvement of the physical functions, but should also incorporate psychological care focusing on the reduction of the fear of falling.

Conflict of interest statement

The authors have no conflict of interest to disclose.

Acknowledgment

This study was supported by a Research Grant of the Ministry from Health and Welfare of Japan and a Grant-in-Aid for Scientific Research B (16300226) from the Japan Society for the Promotion of Science.

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第52回日本老年医学会学術集会記録
〈パネルディスカッション2：高齢者の転倒―その成因の解明と予防対策―〉

5. 転倒予防のための運動介入の効果と課題

金　憲経

Key words：転倒予防，運動介入，身体的要素，可変因子，転倒経験者

（日老医誌　2011；48：39–41）

はじめに

転倒予防戦略を効率的に構築するためには，転倒は転倒関連危険因子（fall-related risk factor）の数と深く関連し，転倒率は危険因子の数とほぼ直線的に増加することへの考察が必要である[1]．つまり，転倒率を下げるためには危険因子の数を減らすことがポイントである（図1）．転倒の抑制策として今日まで提案されている戦略は，服薬管理，教育，環境改善，ヒッププロテクター着用，ビタミンD補充，運動などが挙げられる．

転倒予防のための運動介入の意義

転倒を予防するためには，多くの内的要因のうちの可変要因および外的要因に当てはまる因子を一つ一つ改善していく方法しかない．転倒の危険因子を総合的にまとめた先行研究によれば，転倒の相対的な危険度は筋力低下（RR＝4.4），転倒歴（RR＝3.0），歩行機能低下（RR＝2.9），バランス低下（RR＝2.9）が高く，他に視力障害，関節炎，ADL障害，認知機能障害，年齢80歳以上と関連すると指摘している[2]．なかでも，筋力，歩行，バランスなど身体的要素に関連した要因は，トレーニングや普段からの訓練によって低下を予防し，機能の強化が可能である．すなわち，高齢者の転倒原因の大きな割合を占めている身体的要因は可変因子であることに運動介入の重要な意味がある（図2）．

転倒予防を目的とした運動介入の成果については実に数多く報告されているが，その結果は必ずしも一致せず異なる成果が散見される．転倒予防効果が検証された代表的な介入は，1990年に全米8つの地域で2,400人以上を対象に3年以上行ったFICSIT研究であり[3]，その結果によれば，太極拳を中心としたバランス訓練と筋力トレーニングが最も有効な手法であることが確認されている．さらに，Campbellら[4]は，80歳以上の地域高齢者に筋力，バランス能力改善を目的とした個別処方の在宅運動プログラムを提供した場合でも，転倒予防に有効であったと報告している．一方，Suzukiら[5]は，74～89歳の地域在住高齢者を対象に，2週1回の頻度での集団指導に加えて在宅実践用の個人プログラムを提供する指導を6カ月間行った後，22カ月間の追跡期間中の累積危険度は，対照群0.545，介入群0.136であり，相対危険度は0.25であったことを報告し，監視型に在宅用運動プログラムを加える介入も転倒予防に有効であることを指摘している．一方，Dayら[6]は，70歳以上の高齢者1,090名を対象に，運動，家庭内障害物整備，視力補正の3手法による転倒予防効果を検証した．その結果によれば，単独介入では運動がRR＝0.82（95%CI＝0.70～0.97）と最も効果的であるが，運動に家庭内障害物整備，視力補正を加えるとRR＝0.67（95%CI＝0.51～0.88）に改善することを検証し，多面的支援が転倒予防により効果的であることを提案している．

しかし，Mulrowら[7]は，ADL2つ以上の障害を有するのナーシングホーム入所者194名を対象に4カ月間の運動指導後，1年間の追跡調査を行った結果，移動能力には効果が検証されたが（15.5%改善），転倒率の抑制効果は見られなかった（運動群＝79転倒，対照群＝60転倒，P＝0.11）ことを，Rubensteinら[8]は，7日以内に転倒経験を有する施設長期入所者160名を対象に行った運動指導の結果を分析したところ，介入群の転倒は9%低いものの有意差はなかった．Lordら[9]も，運動介入後に介入群と対照群との間で転倒率には差が見られなかったが（RR＝0.99，95%CI＝0.65～1.50），参加率75%以上のグループでは，転倒率が低くなる傾向が観察された．さらに，Reinschら[10]は，高齢者を対象に行った介入に

The effects of exercise for the prevention of falls
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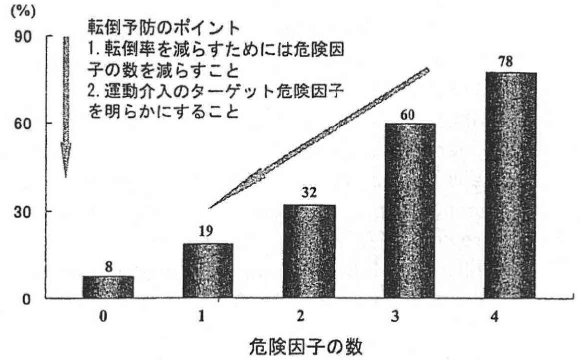

図1　転倒の危険因子の数と転倒率
文献1より改変

転倒危険因子の相対的危険度

危険因子	相対危険度
筋力低下	4.4
転倒歴	3.0
歩行機能低下	2.9
バランス低下	2.9
補助器具の使用	2.6
視力障害	2.5
関節炎	2.4
ADL障害	2.3
うつ病	2.2
認知機能障害	1.8
年齢８０歳以上	1.7

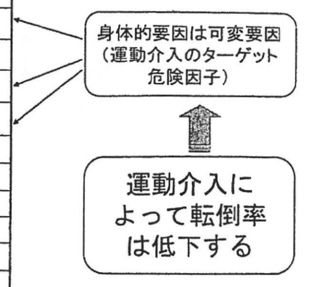

図2　転倒予防のための運動介入戦略
文献2より改変

よって転倒率，初回転倒までの時間，複数回転倒，転倒負傷のみならずバランス能力や筋力，転倒恐怖感，健康度自己評価においても効果が見られなかったことを指摘した上で，介入効果がみられなかった理由としては，運動強度が弱いことや介入頻度が少なかったことであると指摘している．

運動介入のポイント

転倒予防のための運動介入の成果について今日まで報告されている先行研究をまとめると，運動介入効果がないとの研究，身体機能の改善には有効であるが転倒率の減少効果はないとの研究，転倒率の低下のみならず転倒恐怖感の改善効果も得られるとの研究など様々である．これらの結果は，運動介入の際には対象者の諸特性を詳細に把握し，対象者特有の危険因子の改善を目的とした介入になってない場合には，効果が期待できない可能性を示唆するものである．運動介入の時の考慮すべき点は，運動種目，運動強度，運動時間，指導頻度，指導期間，指導形式などである．これらに加えてもう一つ重要なポイントがある．高齢者の転倒原因について調べた結果によれば[11]，高齢者転倒の多くは「歩行中のつまずき」によって発生することである．つまり，高齢者の歩行機能と転倒とは密接に関わり，歩行機能の改善は転倒率抑制に有効であることを示唆するものである．よって，運動介入の際には「歩行機能の改善」および「つまずき防止」を目的とした指導を取り入れるべきであると考える．歩行機能を改善するためには，大腿四頭筋，ハムストリングス，腸腰筋，下腿三頭筋，大殿筋，中殿筋などの重点的な鍛えが必要であり，すり足の改善には前脛骨筋の鍛えが必要不可欠である．次に考慮すべき点は，大腿骨頸部骨折予防である．大腿骨頸部骨折の危険因子は，側面転倒（OR＝3.9），骨密度低下（OR＝1.8），移動障害（OR＝6.4）が指摘され[12]，大腿骨頸部骨折を予防するためには側面バランス機能向上が大切であり，運動指導に当たっては，側面バランス機能の向上を目的とした運動指導が必要であるといえる．

転倒経験者の転倒予防のための運動介入

転倒経験者は転倒経験がない人に比べて身体機能が劣っているとの報告が多く，さらには再転倒の危険因子（RR＝3.0）として指摘されているが，転倒経験者に対する転倒予防戦略の成果についての検討は極めて少ないのが現状である．Skelton ら[13]は，過去1年間で3回以上転倒した65以上の在宅高齢女性81名を運動群50名，対照群31名に分け運動群に週1回，1回当たり60分間の集団指導に家庭用運動プログラムを提供しながら36週間指導したところ，運動指導期間中に発生した転倒数は運動群が対照群に比べて31％も減ったことを指摘し，運動介入は転倒経験者にも有効であると指摘している．筆者らも，2007年度大都市在住70歳以上の男女1,483名を調査し，過去1年間で1回以上転倒者241名（16.3％）に運動介入参加希望者を募集したところ，参加希望者125（51.9％），不参加者116名（48.1％）であった．参加希望者に運動介入を3カ月間実施し，1年間の追跡期間中に発生した転倒率は介入群19.6％，対照群38.3％（Z＝1.979，P＝0.048）であった（図3）[14]．以上のように，再転倒の危険性が高い転倒経験者であっても運動介入へ参加することによって，転倒率の減少効果が得られ，Selton らの効果が追認されたと言える．

運動介入の課題

1．施設入所者に対する効果検証

施設入所者を対象とした研究結果によれば，バランス，

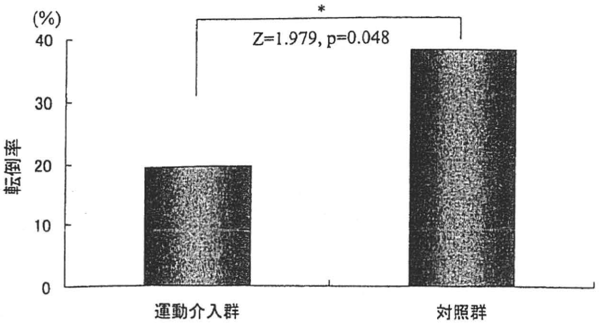

図3　転倒経験者における運動介入後1年間の転倒率
文献14より

筋力，歩行速度などの身体機能や転倒率，転倒恐怖感に改善がみられないとの報告が多く，部分的な改善効果がみられたとの報告はわずかにみられる程度である．長期施設入所者に対する運動介入の有効性については今後さらなる検討が必要といえよう．

2．介入不参加者に対する対応策の確立

前述した通り，転倒経験者でも運動介入への不参加者が48.1％と多いことが問題点である．確かに運動介入に参加し指導を受ければ転倒率は下がることが多くの研究で検証され，筆者も確かめている．しかし，運動介入不参加者の転倒率が上昇した場合には運動介入によって減少した転倒率は不参加者の上昇によって相殺されてしまい，地域全体から見たときの運動介入効果は見えにくくなることも推測される．従って，介入不参加者の特徴を詳細に把握し，不参加者への対応策の確立が最大の課題ともいえる．不参加者への対応策の一つとして「転倒予防手帳」を配布し，間接的介入効果を検討するのも1つの案であると考える．

おわりに

要介護状態になる主な原因として知られている転倒を予防するためには，転倒の可変的な因子を解消していく介入が有効である．中でも，身体的要素の減衰に基づく筋力低下，バランス機能低下，歩行機能低下は普段からの訓練によって低下を最小限に食い止め，機能強化が可能である．すなわち，高齢者の転倒原因の大きな割合を占めている身体的要因は可変因子であることに転倒予防における運動介入の位置づけである．運動介入には，集団指導型，個別処方の在宅介入型が考えられるが，いずれの介入においても，転倒予防効果を認めている．しかし，運動介入には不参加者の割合が高く，不参加者への対策の確立が課題と言える．さらには，施設入所虚弱高齢者の場合は，チームアプローチによる多面的介入によって効果が期待できると指摘されているが，運動介入の有効性については今後さらなる検討が必要である．

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Clinical Section

Gerontology

Gerontology 2010;56:141–149
DOI: 10.1159/000246970

Received: October 20, 2008
Accepted: March 31, 2009
Published online: October 10, 2009

Age-Associated Increase in Abdominal Obesity and Insulin Resistance, and Usefulness of AHA/NHLBI Definition of Metabolic Syndrome for Predicting Cardiovascular Disease in Japanese Elderly with Type 2 Diabetes Mellitus

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Key Words
Diabetes · Obesity · Waist circumference · Insulin resistance · Metabolic disease clustering

Abstract
Background: Management of metabolic syndrome (MetS) seems to constitute an efficient strategy to attain successful ageing. Although the clinical entity of MetS in patients with diabetes mellitus has been discussed, there is very little information on MetS-type cardiometabolic risk factor clustering in diabetic elderly. ***Objective:*** To determine the relationship among age-associated changes in obesity, insulin resistance, and clustering of MetS-type risk factors, in association with vascular complications, in Japanese elderly with type 2 diabetes. ***Methods:*** A cross-sectional study was conducted of 812 diabetic elderly enrolled in the Japanese Elderly Diabetes Intervention Trial. Information on diabetes, blood examinations and complications was obtained. Abdominal obesity, insulin resistance and prevalence of MetS risk factor clustering, defined by three sets of criteria from the International Diabetes Federation (IDF), the Japanese Society of Internal Medicine (JSIM), and the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI), were analyzed. ***Results:*** Waist circumference and insulin resistance estimated by homeostasis model assessment insulin resistance (HOMA-IR) increased with age, followed by a partial decrease at age 80 and over. Prevalence of IDF-MetS and JSIM-MetS also increased with age at least until the age of 80, whereas the incidence of AHA/NHLBI-MetS did not show any apparent age changes. There was a significant crude linear association between waist circumference and HOMA-IR, which was highly elevated in IDF and AHA/NHLBI overlapping with MetS, and also elevated in AHA/NHLBI without abdominal obesity. Although IDF-MetS and JSIM-MetS, which specify abdominal obesity, did not always appear to be associated with cardiovascular diseases, AHA/NHLBI-MetS, comprising both abdominal obesity and non-abdominal obesity, independently correlated with coronary heart disease and stroke after adjustment for other risk factors of atherosclerotic diseases. ***Conclusion:*** There was an age-associated increase in the prevalence of abdominal obesity and insulin resistance in elderly diabetic Japanese subjects, with a clear relationship between waist circumference and insulin resistance. However, insulin resistance was elevated not only in cases with but also in those

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without abdominal obesity if accompanied by clustering of metabolic disorders. The AHA/NHLBI definition of MetS proved to be the most useful to predict cardiovascular disease in the diabetic elderly.

Introduction

Metabolic syndrome (MetS) consists of multiple, interrelated risk factors of metabolic origin that appear to directly promote the development of cardiovascular disease. Recently, MetS has been reported to be associated with impaired activities of daily living (ADLs) and cognitive decline of the elderly [1, 2]. Thus, management of risk factors and prevention of MetS seem to constitute an efficient strategy to attain successful ageing. Although insulin resistance and visceral adiposity could play a pivotal role in promoting atherosclerosis, the real cause may be a more complex interaction between genetic and environmental factors [3, 4].

The clinical usefulness of MetS for risk prediction for individuals with type 2 diabetes remains a matter of debate. It has been reported that insulin resistance and MetS are predictive of accelerated atherosclerosis in type 2 diabetic patients [5–14]. On the other hand, a recent reappraisal of MetS endorsed by the American Diabetes Association and the European Association for the Study of Diabetes argues that MetS is an entity of little or no prognostic use for diabetic patients [15]. They emphasized that it remains unclear whether identification of MetS confers a clinical advantage over identification and treatment of its individual components. Although the term MetS may not be applicable to diabetic subjects, even detractors agree that there are diabetic elderly who have increased insulin resistance associated with MetS-type cardiometabolic risk factor clustering [5–14].

Moreover, ageing is associated with increased insulin resistance in addition to type 2 diabetes [16]. Thus, the impact of abdominal obesity on insulin resistance and clustering of metabolic risk factors in diabetic elderly remains unknown. To date, for Asian elderly with type 2 diabetes, there is limited information on age-associated changes in abdominal obesity, insulin resistance and clustering of metabolic risk factors, and their association with vascular complications.

To address the need for elucidation concerning metabolic risk factor clustering in diabetic elderly, we conducted a large-scale prospective study of the Japanese Elderly Diabetes Intervention Trial (J-EDIT) [17, 18]. The questions we addressed were: (1) prevalence of abdominal obesity, insulin resistance, and MetS-type risk factor clustering as defined by different sets of criteria; (2) possible connections between abdominal obesity and insulin resistance, and (3) the predictive power of MetS-type clustering of metabolic risk factors for cardiovascular diseases in diabetic elderly. To answer these questions, we analyzed the baseline measures of the J-EDIT.

Methods

Participants

J-EDIT started in 2001 with an enrolment of 1,173 diabetic subjects aged 65 years or over and with serum HbA1c levels of ≥7.0% from 42 institutes in Japan. The J-EDIT protocol, which is in accordance with the provisions of the Declaration of Helsinki, received ethical approval from the institutional review boards of all of the participating institutes. Written informed consent was obtained from all patients. All examinations relevant for this study were completed by 812 subjects, 371 of whom were men. The remaining 361 subjects were excluded because some of their data were missing.

Diagnostic Criteria for MetS

In this study, we applied the three different sets of criteria proposed for the diagnosis of MetS by the International Diabetes Federation (IDF), the Japanese Society of Internal Medicine (JSIM) and the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI) [19–21]. According to IDF and JSIM criteria, there is a strong correlation between abdominal obesity and insulin resistance, which makes the presence of abdominal obesity a condition for diagnosis of MetS [19, 20]. A Japanese study concluded that a visceral fat area in excess of 100 cm^2 measured by means of CT scanning corresponds to a waist circumference of 85 cm for men and ≥90 cm for women [22]. In 2005, moreover, the IDF recognized specific cutoffs by sex and ethnicity [23]. However, new data support the use of alternative waist circumference cutoffs for the prediction of cardiovascular complications [24–26]. In 2007, the IDF recommended new waist circumference cutoffs for Japanese, 90 cm for men and 80 cm for women [19]. However, these cutoffs for waist circumference in the definition of MetS for Japanese have remained a matter of debate. For our study, we therefore adopted two criteria, one from the IDF (2007) and one from the JSIM. On the other hand, AHA/NHLBI has introduced alternative criteria, which have the advantage of avoiding emphasis on a single cause [21]. The resulting three definitions for MetS are as follows.

(1) The IDF definition of MetS (IDF-MetS) specifies abdominal obesity with waist circumference cutoffs of ≥90 cm for men or ≥80 cm for women plus any one of the following factors [19]: (a) elevated triglyceride (≥150 mg/dl) or specific treatment for this lipid abnormality; (b) reduced HDL-cholesterol of <40 mg/dl for men or <50 mg/dl for women, and (c) elevated systolic blood pressure (≥130 mm Hg) or diastolic blood pressure (≥85 mm Hg) or treatment for previously diagnosed hypertension.

Table 1. Demographic and clinical parameters of the patients

	Male	Female	All subjects
n	371	441	812
Age, years	71.4 ± 4.5	72.0 ± 4.6	71.8 ± 4.6
Duration of diabetes, years	16.7 ± 10.2	15.7 ± 8.8	16.2 ± 9.5
Systolic blood pressure, mm Hg	137.1 ± 15.8	138.6 ± 17.3	137.9 ± 16.7
Diastolic blood pressure, mm Hg	76.2 ± 9.6	75.5 ± 10.0	75.8 ± 9.9
HbA1c, %	8.0 ± 0.9	8.0 ± 0.9	8.0 ± 0.9
Fasting plasma glucose, mg/dl	169.7 ± 50.5	165.1 ± 50.7	167.2 ± 50.6
Fasting plasma insulin, μU/ml	9.3 ± 10.0	10.2 ± 8.5	9.8 ± 9.3
Urine Alb, mg/g Cr	226.4 ± 597.9	184.5 ± 499.7	203.7 ± 546.8
Serum cholesterol, mg/dl	192.7 ± 31.2	209.5 ± 34.5	201.8 ± 34.1
Serum HDL-C, mg/dl	52.9 ± 15.5	60.3 ± 19.4	56.9 ± 18.1
Serum LDL-C, mg/dl	114.9 ± 28.0	123.7 ± 32.0	119.7 ± 30.5
Serum triglyceride, mg/dl	129.2 ± 84.1	129.4 ± 66.4	129.3 ± 74.9
Current smokers, %	28.4	5.8	16.2
OHA use, %	62.5	61.7	62.1
Insulin use, %	25.3	31.1	28.5
Medication for hypertension, %	47.3	61.9	55.1
Medication with fibrates, %	3.2	4.3	3.8
Medication with statin, %	18.9	43.1	32.0
History of CHD, %	15.5	15.6	15.6
History of stroke, %	14.7	11.3	12.9

Data are presented as means ± SD or as percentages. OHA = Oral antihyperglycemic agents; CHD = coronary heart disease.

(2) The JSIM definition of MetS (JSIM-MetS) specifies abdominal obesity with waist circumference cutoffs of ≥85 cm for men or ≥90 cm for women, plus any one of the following factors [20]: (a) elevated triglyceride (≥150 mg/dl) or reduced HDL-cholesterol (<40 mg/dl) or specific treatment for these lipid abnormalities, and (b) elevated systolic blood pressure (≥130 mm Hg) or diastolic blood pressure (≥85 mm Hg) or treatment for previously diagnosed hypertension.

(3) The AHA/NHLBI definition of MetS (AHA/NHLBI-MetS) specifies two or more of the following conditions [21]: (a) waist circumference of ≥90 cm for men or ≥80 cm for women; (b) elevated triglyceride (≥150 mg/dl) or specific treatment for lipid abnormality; (c) reduced HDL-cholesterol of <40 mmol/l for men or 50 mmol/l for women, and (d) elevated systolic blood pressure (≥130 mm Hg) or diastolic blood pressure (≥85 mm Hg) or treatment for previously diagnosed hypertension.

Assessment of Diabetes Mellitus and Complications

Information about diabetes mellitus, blood examinations and complications were obtained from clinical charts. Waist circumference was measured at the umbilicus level. Information regarding cigarette smoking was collected using a standardized questionnaire.

After overnight fasting, blood samples were taken by vein puncture to assess serum levels of glucose, HbA1c, total cholesterol, triglyceride, and HDL-cholesterol. Insulin resistance was assessed from levels of fasting glucose and insulin concentration by means of the homeostasis model assessment (HOMA) formula: fasting insulin (μU/ml) × fasting glucose (mg/dl)/405 [27]. This method was not applicable to subjects treated with insulin. Serum LDL-cholesterol levels were calculated using Friedewald's equation, except for triglyceride levels of >400 mg/dl, in which case the LDL cholesterol data were recorded as 'missing'.

Information about a previous history of coronary heart disease (CHD) and stroke and findings from a 12-lead electrocardiogram (ECG) were obtained for all patients to assess cardiovascular disease at baseline. CHD was considered to be present when diabetic patients had at least one of the following: a history of myocardial infarction and angina characterized by a typical clinical picture (chest pain, chest oppression, dyspnea, typical ECG alteration). Stroke events were defined as a constellation of neurological deficits of sudden or rapid onset for which there was no apparent cause other than a vascular accident. Cases with asymptomatic lesions detected by brain imaging were not included.

Statistical Analysis

Data are presented as means ± SD or as percentages unless otherwise specified. Association of waist circumference with HOMA insulin resistance (HOMA-IR) was tested using simple and multiple logistic regression. Variables among the MetS subgroups were compared using ANOVA and statistical differences were tested with Dunnett's statistical test. Backward logistic regression analysis was used to calculate the adjusted odds ratio (OR) and 95% confidence interval (CI) for risk factors with cardiovascular diseases. The SAS software package (Version 8.0; SAS, Cary, N.C., USA) was used for all analyses. $p < 0.05$ was considered significant.

Table 2. Age-associated changes in BMI, waist circumference, HOMA-IR, and prevalence of MetS risk factors

	Men, age group				Women, age group			
	65–69	70–74	75–79	80–85	65–69	70–74	75–79	80–85
BMI	23.8 ± 3.2	23.9 ± 3.1	23.9 ± 3.1	23.6 ± 2.7	23.6 ± 3.5	24.1 ± 3.8	24.5 ± 3.7	22.8 ± 3.3
Waist circumference, cm	85.8 ± 8.9	85.0 ± 8.1	87.6 ± 8.1	88.3 ± 10.0	80.6 ± 10.4	82.7 ± 10.7	84.5 ± 11.2	79.6 ± 10.2
HOMA-IR	3.81 ± 4.0	3.37 ± 3.1	4.37 ± 5.8	2.83 ± 2.0	3.17 ± 2.7	3.49 ± 3.0	4.80 ± 3.6	3.54 ± 4.1
IDF-MetS, %	28.6	30.4	33.3	42.1	47.9	59.6	59.6	46.9
JSIM-MetS, %	51.7	47.4	59.7	68.4	19.4	23.0	31.7	25.0
AHA/NHLBI-MetS, %	56.5	52.6	59.7	57.9	72.2	83.2	80.8	65.6
Hypertension, %	79.6	74.6	84.5	84.2	77.8	87.6	91.3	96.9
IDF and AHA/NHLBI								
Low HDL-C, %	38.1	30.6	35.2	31.6	60.4	65.8	65.4	46.9
High triglyceride, %	26.5	30.6	25.4	36.8	29.2	36.6	30.8	25.0
JSIM dyslipidemia, %	36.1	37.3	33.8	47.4	30.6	39.1	32.7	28.1

Data are presented as means ± SD or as percentages. BMI = Body mass index; HOMA-IR = homeostasis model assessment, insulin resistance; MetS = metabolic syndrome; IDF = International Diabetes Federation; JSIM = Japanese Society of Internal Medicine; AHA/NHLBI = American Heart Association and the National Heart, Lung, and Blood Institute.

Results

Age-Associated Increase in Abdominal Obesity, Insulin Resistance and MetS-Type Risk Factor Clustering

Demographic and clinical parameters of the 812 study participants are listed in table 1. Age-associated changes in BMI, waist circumference, and HOMA-IR are listed in table 2. BMI did not show any apparent changes for men, although waist circumference increased with age. Waist circumference also increased for women, followed by a decrease at the age of 80 or over. HOMA-IR similarly increased with age, but decreased from the age of 80 for both men and women. The increase in insulin resistance seemed to correlate with the age-associated increase in abdominal obesity of diabetic elderly.

The overall prevalence of MetS-type risk factor clustering based on IDF, JSIM and AHA/NHLBI criteria was 44.0, 37.1 and 67.7%, respectively. The incidence of IDF-MetS and JSIM-MetS, which specify abdominal obesity, increased with age, but decreased at age 80 or over for women (table 2). In contrast, the prevalence of AHA/NHLBI-MetS did not show any apparent change with ageing.

As for the individual components of MetS, the prevalence of hypertension was highest and increased with age. Among diabetic elderly aged 80–85 years, hypertension was found in 84.2% of men and 96.9% of women. The prevalence of low HDL-cholesterol also increased with age, but started to decrease at the age of 80 and over.

We also investigated whether diabetic patients with a longer history of diabetes and/or more serious hyperglycemia might show an increased prevalence of MetS-type risk factor clustering, but no such trend could be found in any type of criteria-defined MetS (data not shown).

Possible Connections between Abdominal Obesity and Insulin Resistance

Overall, HOMA-IR was 4.2 ± 5.0 for diabetic elderly. The relationship between waist circumference and insulin resistance is shown in figure 1. Simple regression analysis showed that log-transformed HOMA-IR was associated with waist circumference in a crude linear manner (coefficient = 0.051, $p < 0.0001$, $R^2 = 0.105$ for men; coefficient = 0.034, $p < 0.0001$, $R^2 = 0.116$ for women). This was demonstrated by an increase in HOMA-IR of 1.1 for men and 0.6 for women for every 10-cm increment in waist circumference. After adjustment for sex, age, systolic blood pressure, HbA1c, triglyceride, and HDL-C, the association remained statistically significant (coefficient = 0.034, $p < 0.0001$).

For any of the three definitions, HOMA-IR was higher for subjects with MetS than for those without MetS (4.34 ± 3.65 for IDF-MetS and 3.21 ± 3.50 for non-IDF-MetS, p = 0.0003; 4.33 ± 3.95 for JSIM-MetS and 3.30 ± 3.33 for non-JSIM-MetS, p = 0.0022; 4.03 ± 3.58 for AHA/NHLBI-MetS and 3.04 ± 3.57 for non-AHA/NHLBI-MetS, p = 0.0022).

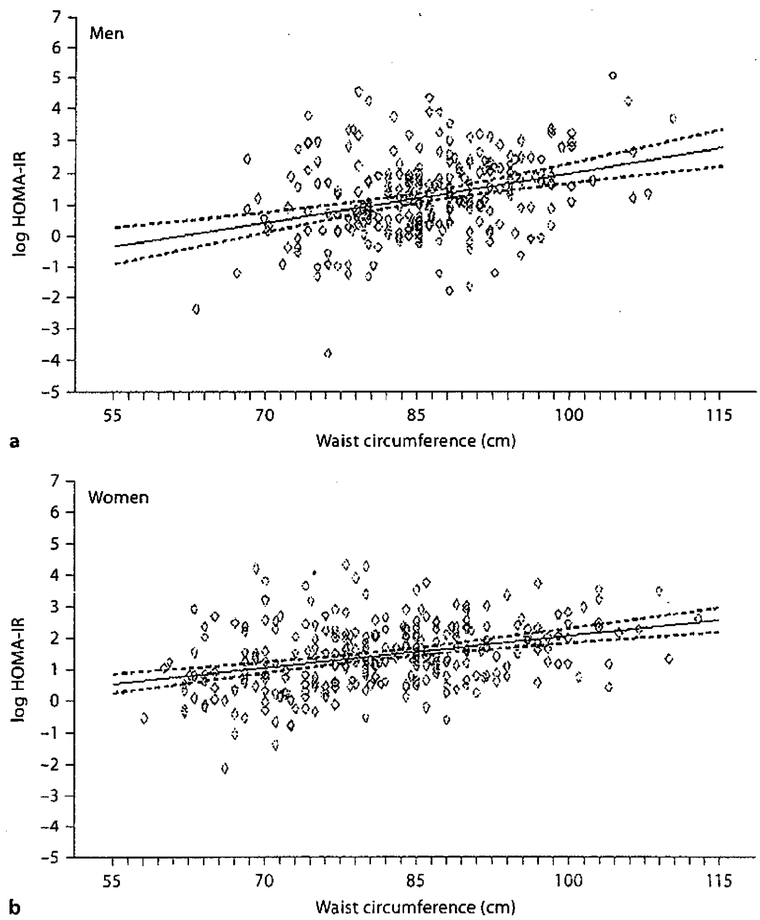

Fig. 1. Relationship between waist circumference and insulin resistance. Association of HOMA-IR with waist circumference of men (**a**) and women (**b**) in the J-EDIT. Log-transformed HOMA-IR (log HOMA-IR) was associated with waist circumference in a crude linear manner (coefficient = 0.051, $p < 0.0001$, $R^2 = 0.105$ for men; coefficient = 0.034, $p < 0.0001$, $R^2 = 0.116$ for women).

It has been proposed that HOMA-IR is useful for estimating insulin resistance of type 2 diabetic patients [28], but the degree of association between HOMA-IR and clamp insulin resistance for diabetic patients treated with oral antihyperglycemic agents of the class insulin secretagogues has remained unclear. In this connection, Emoto et al. [29] have reported that HOMA-IR strongly correlates with clamp insulin resistance in type 2 diabetic patients treated with sulfonylureas (SUs) as well as in those treated with diet alone. Furthermore, Spearman's correlation coefficients for HOMA-IR and waist circumference were similar for subjects taking SU drugs and those who had used neither SU drugs nor glinides (data not shown). Such evidence indicates that it seems likely that waist circumference is associated with insulin resistance in diabetic elderly, regardless of treatment with oral antihyperglycemic agents of the class insulin secretagogues.

Insulin Resistance of Metabolic Factor Clustering with and without Abdominal Obesity

We compared the clinical characteristics of IDF-MetS and AHA/NHLBI-MetS by dividing the study population into 3 subgroups, non-MetS, AHA/NHLBI-only, and IDF&AHA/NHLBI (table 3). There was no difference in age among the subgroups. HOMA-IR was especially elevated in the IDF&AHA/NHLBI group, as was waist circumference. Interestingly, in the AHA/NHLBI-only group, HOMA-IR was moderately elevated without an accompanying increase in waist circumference. Furthermore, the mean duration of diabetes for MetS with overlapping patterns was significantly shorter than that for

Table 3. Clinical characteristics of subgroups of IDF-MetS and AHA/NHLBI-MetS risk factor clustering

	Non-MetS	AHA/ NHLBI only	IDF&AHA/ NHLBI
Number	263	192	357
Age, years	71.9 ± 4.7	71.0 ± 4.5	72.1 ± 4.5
Waist circumference, cm	78.2 ± 7.9	77.7 ± 6.8	91.4 ± 7.3*
HOMA-IR	3.04 ± 3.6	3.46 ± 3.4	4.34 ± 3.7*
Duration of diabetes, years	16.1 ± 10.3	14.0 ± 8.2	13.6 ± 8.7‡

For abbreviations see table 2. Data are means ± SD or actual numbers.

* $p < 0.001$, † $p = 0.004$, ‡ $p = 0.012$, in comparison with non-MetS.

non-MetS. These results suggest that there are two distinct ways for insulin resistance to increase in diabetic elderly, one is in association with abdominal obesity and the other is not relevant to abdominal obesity.

Association of MetS-Type Risk Factor Clustering with Cardiovascular Disease

We examined the independent association of MetS-type risk factor clustering with cardiovascular diseases (table 4). Because sex is reportedly an independent factor associated with MetS [30–32], MetS and sex were included in the independent variables, while the other risk factors for atherosclerotic disease, such as age, HbA1c, duration of diabetes, smoking, total cholesterol, LDL-cholesterol, triglyceride, systolic blood pressure and diastolic blood pressure, were analyzed with backward stepwise regression. Age was found to be consistently associated with CHD, while JSIM-MetS and AHA/NHLBI-MetS, but not IDF-MetS, were also associated with CHD. When MetS was eliminated from the independent variables, age and diastolic blood pressure proved to be significantly associated with CHD, suggesting these factors independently correlate with CHD in diabetic elderly. For stroke, AHA/NHLBI-MetS was identified as a predictive factor. When MetS was eliminated from the independent variables, sex (men) and triglyceride showed a significant correlation with stroke. On the other hand, IDF-MetS and JSIM-MetS, which both specify the presence of abdominal obesity for MetS, were not associated with stroke. These results indicate that MetS of AHA/NHLBI definition is the most consistent predictor for CHD and stroke for diabetic elderly, even after adjustment for the risk factors of age, sex, blood pressure, dyslipidemia, and indices of diabetes.

Table 4. Association of MetS and other risk factors with cardiovascular disease

Previous history of CHD			Previous history of stroke		
	OR	95% CI		OR	95% CI
IDF					
MetS	1.44	0.91–2.28	MetS	1.16	0.70–1.92
Sex	1.39	0.88–2.19	Sex	1.69	1.03–2.75
Age	1.06	1.01–1.12	Age	1.05	0.99–1.10
DBP	0.98	0.95–0.99	TG	1.01	1.00–1.01
			DM duration	1.25	0.89–1.75
JSIM					
MetS	1.80	1.14–2.85	MetS	1.32	0.79–2.19
Sex	1.10	0.70–1.73	Sex	1.51	0.92–2.47
Age	1.06	1.01–1.11	Age	1.05	0.99–1.10
DBP	0.97	0.95–0.99	TG	1.01	1.00–1.01
			DM duration	1.27	0.90–1.78
AHA/NHLBI					
MetS	1.90	1.13–3.19	MetS	1.86	1.07–3.24
Sex	1.48	0.94–2.33	Sex	1.84	1.13–3.00
Age	1.06	1.01–1.12	Age	1.05	0.99–1.11
DBP	0.97	0.95–0.99			
Factors other than MetS					
Sex	1.26	0.82–1.95	Sex	1.63	1.01–2.61
Age	1.01	1.01–1.12	Age	1.05	0.99–1.11
DBP	0.98	0.96–0.99	TG	1.01	1.00–1.01
			DM duration	1.25	0.89–1.75

MetS = Metabolic syndrome; CHD = coronary heart disease; SBP = systolic blood pressure; DBP = diastolic blood pressure; TG = triglyceride; DM = diabetes mellitus. For other abbreviations, see table 2.

The association of IDF-MetS, JSIM-MetS and AHA/NHLBI-MetS with cardiovascular disease was examined. MetS and sex were included in the independent variables, and age, HbA1c, duration of diabetes, smoking, total cholesterol, LDL-cholesterol, TG, SBP and DBP were analyzed with backward stepwise regression.

Discussion

This J-EDIT study first provided evidence of MetS-type risk factor clustering in Asian (Japanese) elderly with type 2 diabetes. Several new findings are reported: (1) abdominal obesity, insulin resistance and prevalence of MetS-type risk factor clustering evidently increased with age, but somewhat decreased at the age of 80 and over; (2) overall insulin resistance was substantially elevated in diabetic elderly [28, 30], and there was a significant crude linear association between waist circumference and insulin resistance; (3) insulin resistance was elevated not only in cases with but also without abdominal