

Fig. 2 No correlation was found between correct diagnosis rate and the number of complicating prevalent fractures. a Diagnosis rate when divided into one of six groups. b Diagnosis rate when divided into one of two groups

(p<0.0001). Similar results were obtained even after adjustment had been made for variation between the examiners. However, this significant difference disappeared after age, body weight, and lumbar BMD had been adjusted for. The same results were obtained in the incident fracture group with prevalent fractures, but in this case a significant difference was seen after correction in the incident fracture group without prevalent fractures (p=0.0455) (Table 3).

#### The primary osteoporosis diagnostic criteria

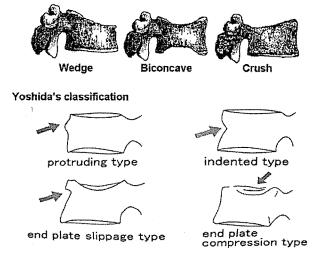


Fig. 3 The morphological classifications used were the primary osteoporosis diagnostic criteria of Genant [8] and Yoshida's [9] classification. Yoshida's criteria is for incident fractures and classified in four types as follows: protruding type, the anterior bone cortex disrupted protrudes anteriorly; indented type, the anterior bone cortex disrupted indents posteriorly; end plate slippage type, the anterior edge of the end plate disrupted displaces anteriorly; end plate compression type, the center of the end plate disrupted indents and depressed

#### Yoshida's classification

When Yoshida's classification was applied, the correct diagnosis rate was high for intended and protruding types of fractures (p<0.0001). The correct diagnosis rate was significantly higher in the incident fracture group without prevalent fractures even when there were morphological changes (wedge, intended and protruding type) in the anterior bone cortex. Conversely, the correct diagnosis rate was low in the incident fracture group with prevalent fractures, end plate compression and slippage type fractures with no morphological changes in the anterior bone cortex, and in "miscellaneous" cases that belonged to no category and had almost no morphological change.

#### Odds ratios affected the rate of correct diagnosis

Odds ratios (ORs) were investigated for factors that would affect the correct diagnosis rate, including age, body weight, lumbar vertebrae BMD, and examiner ability. In an overall investigation, age (OR=0.660), body weight (OR=2.082), and examiner ability (p=0.0205) affected the correct diagnosis rate. A younger age and greater body weight resulted in higher correct diagnosis rates, and results were also affected by the examiner's ability. None of these factors had an effect in the non-incident fracture group. Significant variation is seen in examiner's ability in Fig. 1, but not to the extent that results were affected (p=0.0709). In the fracture groups, both body weight (OR=2.206) and examiner ability (p=0.0039) affected the results. This was also seen in the incident fracture group without prevalent fractures alone, but in the incident fracture group with prevalent fractures alone only lumbar BMD had an effect (OR=1.574) (Table 4).

#### Discussion

The prevalence rate of spinal fracture is thought to be 117 people per 100,000 in the population [10], and the lifetime

Table 3 Diagnosis rate<sup>a</sup> according to the morphological classifications

Genant classific	ation					
Fracture type	Numbers	Diagnosis rate – total fracture group	Numbers	Diagnosis rate – without prevalent fractures	Numbers	Diagnosis rate without prevalent fractures
Wedge	22	40.90%	6	63.30%	16	32.50%
Crush	9	26.70%	3	53.30%	6	13.30%
Biconcave	17	24.70%	4	40.00%	13	20.00%
Other	40	18%	12	30%	28	12.80%
$a^b$	p<0.0001		p=0.0011		p<0.0011	
b	p<0.0001		•		-	
С	p=0.9123		p=0.0455		p=0.9516	
Yoshida's classi	fication		-			
Fracture type	Numbers	Diagnosis rate – tota fracture group	al Numbers	Diagnosis rate – without prevalent fractures	Numbers	Diagnosis rate without prevalent fractures
End plate slip- page	17	29.40%	7	45.71%	10	18.00%
Intended	8	46.70%	2	90.00%	6	40.00%
protruding	9	60%	4	80.00%	5	44.00%
End plate compression	6	10%	2	10%	4	10.00%
Other	48	16.20%	10	22.91%	38	14.21%
$a^b$	p<0.0001		p=0.0016		p=0.0173	
ь	p<0.0001		-		4	
С	p=0.4708		p=0.0455		p=0.6953	

<sup>&</sup>lt;sup>a</sup>The correct diagnosis rate was higher in the incident fracture group without prevalent fractures even when there were morphological changes in the anterior bone cortex. In seven cases, we were unable to classify the morphology because of indistinctness ba, Unadjusted p value; b, p value adjusted with examiners; c p value adjusted with age, weight, BMD and examiners

risk of spinal fracture in women over the age of 50 rises to about 40% [11]. Vertebral body fractures result in pain and functional restrictions, and provoke a marked decrease in quality of life [12, 13]. Therefore, early prevention of spinal fractures and accurate diagnosis and treatment are crucial. There are various reports on the diagnosis of incident spinal fracture [14], but a diagnostic gold standard has yet to be established. Nearly all institutions first take X-P images for patients presenting with lumbar pain. However, it is difficult to determine from X-P images the presence and location of incident fragility fractures in elderly patients with osteoporosis at the time of injury; it is even more difficult when the patient has prevalent fractures. Furthermore, incident fractures are defined as those vertebral bodies that show distinct morphologic changes or osteosclerosis change on the follow-up X-P

images. Consequently, we usually cannot detect incident fractures at the early stage of diagnosis.

With respect to the effectiveness of X-Ps for lumbar pain disease in general, David et al. reported that 17.8% of patients in an emergency department received unnecessary lumbar X-Ps [15], while Khoo et al. reported that 90.5% of AP views on X-Ps have no benefit and were effective only in assessing the sacroiliac joint [16]. Thus, establishing a diagnosis for lumbar pain is difficult with X-P alone, and most cases require MRI. Many reports attest to the high diagnostic accuracy of MRI, and it continues to be more useful tool in diagnosing spinal fracture [4–6]. In MRI images, fractures are defined so that an acute fracture associated with hemorrhage and edema increases the focal water content and thus increases the signal on T2-images. With an osteoporotic fracture, the hemorrhage will be organized and the edema will decrease, giving a low to

Table 4 Odds ratios of factors that would affect the correct diagnosis rate

Factors	Total		Non-incider group	nt fracture	Total frac	ture group	Without prevalent fractures		With prevalent fractures	
	Odds ratio	p value	Odds ratio	p value	Odds ratio	p value	Odds ratio	p value	Odds ratio	p value
Age	0.66	<0.001	0.781	0.2817	1.053	0.7098	1.02	0.9291	1.254	0.1966
Body weight	2.082	< 0.001	0.661	0.0876	2.206	< 0.001	3.002	< 0.0001	1.42	0.1303
Lumbar BMD	1.246	0.072	1.108	0.676	1.043	00.7873	0.65	0.0584	1.574	0.0478
Ability of the examiner	_	0.0205	-	0.0709	-	0.0039		0.0349	-	0.1163

Results were affected by examiner ability, age and body weight

intermediate signal intensity on T2-weighted images. It has already been reported that femoral neck fractures cannot be judged on X-P images and that MRI diagnosis is useful in cases of occult fracture. Pandey et al. reported that fractures are not discovered on X-P images and that even on MRI images, 30% show no fracture [17], while Rizzo et al. reported that occult fractures were detected on MRI in 36 of 62 patients (58%) [18].

With respect to spinal disease as well, Nakano et al. investigated the diagnostic accuracy of MRI for incident vertebral fractures. They took vertebral bodies showing signs of crush and bone sclerosis on follow-up X-P images to indicate true incident fractures and reported that the diagnostic sensitivity and specificity of MRI were 99.0% and 98.7 %, respectively [19, 20]. They also reported that based on diagnosis with MRI it was possible to diagnose with precision a fracture in the early period of onset. In addition, Kanchiku et al. reported that the diagnostic rate of the fractured vertebral body was 98% by MRI, which was higher than the 87% for plain radiography (p=0.006); in patients for whom no posterior wall injury was seen on X-P imaging at the time of the injury, intraspinal protrusion of the posterior wall of the vertebral body was diagnosed in 37% using MRI [21]. Eugene et al. reported that twice as many spinal diseases were detected when using MRI as when diagnosis was made from X-P imaging [2]. Thus, MRI is considered to be reliable in the diagnosis of incident fragility fracture. However, this high diagnostic accuracy also gives rise to some problems. Rupp et al. reported that in distinguishing between tumor and compression fracture on MRI images, compression fracture can only be diagnosed in those patients that have completely maintained normal marrow within the vertebrae and that it is difficult to make a distinction, due to changes in contrast effect and intensity, over multiple vertebrae or invasion to the posterior vertebral body wall [22]. In addition, Cuenod et al. reported that at 2 months after a spinal fracture is sustained, changes in brightness on MRI images have completely returned to normal in only 13% of the cases [23], indicating the possibility that old fractures can be mistaken for incident fractures. Equipment limitations at some institutions and economic problems make it impossible to conduct MRI with all patients. Jefferey et al. compared MRI in the acute phase of lumbar pain with X-P over the clinical course and concluded that no cost benefit was achieved [24]. Thus, several problems are also encountered with the use of MRI in diagnosis.

Based on all of the points raised above, we re-examined X-P diagnosis and investigated whether the correct diagnosis rate with X-P in the initial examination could be improved. To our knowledge, this type of comparison has not been carried out to date, however, a search of the literature has revealed that various data sets are available on diagnosis rates for incident fractures with X-P. In a comparison of local and central readings, Pierre et al. reported a correct diagnosis rate of 95% in the non-fracture group and 66% in the fracture group [25]. Hachiya et al. reported a correct diagnosis rate of 43%, false positives in 41% of the cases, and false negatives in 16% [26]. Nakano

et al. reported a correct diagnosis rate of 51.5% [27], while Kanchiku et al. reported a high correct diagnosis rate of 87% [21]. However, factors such as unspecified measurement conditions, a small number of examiners, or non-uniform skill levels of examiners in these studies make them inadequate for the establishment of a correct diagnosis rate.

In the present study, a strict diagnosis was made together with radiologists, the ability of five orthopedists to interpret X-Ps was determined in advance to be uniform, and three groups were compared. The results of this analysis showed the correct diagnosis rate to be 51.5%, which did not differ greatly from the reports of previous investigators. However, the mean correct diagnosis rate for incident vertebral fracture group was 24.8%, and it was even lower – 16.8% – in the group with prevalent fractures. The correct diagnosis rate decreased in order of non-incident fracture group (highest), the incident fracture group without prevalent fractures, and the incident fracture group with prevalent fractures (lowest), a result which demonstrates anew the difficulty of diagnosing the location of fractures in the daily clinical setting. Moreover, after correcting for various factors, we found that there was a significant interexaminer variation in all groups. This seems to indicate that the ability of an examiner to interpret radiographs is reflected in the correct diagnosis rate. In an examination based on the number of prevalent fractures, the correct diagnosis rate did not drop as the number of prevalent fractures increased, and no correlation was found. This finding that the number of prevalent fractures does not exert an effect is intriguing. Thus, even with prevalent fractures over multiple vertebrae, it is assumed that with diligence, incident fractures can be detected.

The previously mentioned criteria of Genant et al. were used in the analysis by morphological classification [8]. These criteria are commonly used in the diagnosis of osteoporotic vertebral body fractures. However, 45.5% of the cases in our study did not fit any type in these classifications, bringing some doubt to the judgments that have been made to date. We therefore conducted the investigation using these criteria in conjunction with Yoshida's classifications [9]. A high correct diagnosis rate was obtained for wedge type fractures with the diagnostic criteria for primary osteoporosis, and for protruding and indented type fractures with Yoshida's criteria; however, the correct diagnosis rate was low with the remaining types of fractures. Thus, a key to raising the correct diagnosis rate for incident fragility fractures may be to focus sufficient attention on morphological changes in the anterior bone cortex when diagnosing from X-P

In this investigation of factors influencing the correct diagnosis rate of osteoporotic vertebral body fractures, we found age, body weight, and examiner ability had an overall effect. The negative correlation seen with age, in which the correct diagnosis rate decreased as age increased, and the decrease in the correct diagnosis rate with lower body weight are understandable, but the finding that BMD did not exert an effect was intriguing. Moreover, the

finding that the ability of the examiner to interpret radiographs was reflected in the correct diagnosis rate indicates the importance of continuing efforts to improve ability

Several points remain for future study, including the facts that the present study was a retrospective study and that the diagnosis was made without questioning the patients or pathological findings. Based on the results presented here, an investigation of how repeat readings will change the correct diagnosis rate should also be made. In any case, the finding that the correct diagnosis rate was low, even when made by orthopedists experienced in reading radiographs, is a finding that should be taken into consideration in the normal diagnosis of incident spinal fragility fractures with X-Ps only, and may be important in identifying keys for the development of new diagnostic criteria and more accurate diagnoses. The present study indicates the importance of not only improving the ability of examiners to interpret radiographs but also of the attention that should be paid to morphological changes in the anterior bone cortex during examinations.

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特集 介護予防をめぐって

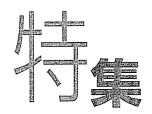
# 転倒予防

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# 総合リハビリテーション

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# 転倒予防\*

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Key Words:高齢者,転倒予防事業,実態,効果

## はじめに

高齢者が日常生活上で介護の必要な状況となる原因は、脳血管疾患が最多であるが、それに次ぐものに、高齢による衰弱、転倒・骨折、認知症などがある<sup>1)</sup>. そのため、転倒予防は、要介護状態の予防を検討する際には、きわめて重要な問題の一つと考えられる. 2006 年度から施行された改正

介護保険法においても、転倒予防は介護予防サービスの一つとして、大きな比重が置かれている。 筆者らは、厚生労働省長寿科学総合研究事業「高齢者における効果的な転倒予防活動事業の推進に関する研究」において、自治体が行う転倒予防事業の内容や効果に関する調査を実施した。介護保険法が改正される前の状況であるが、本稿では、その結果の一部を紹介する。

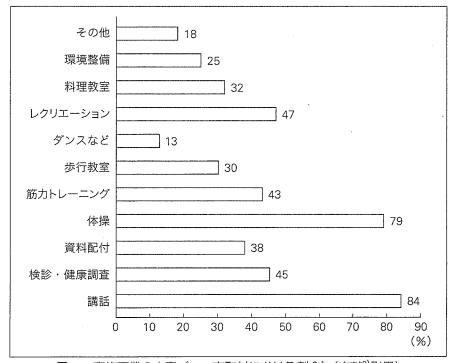


図 1 実施事業の内容(151 市町村における割合)(文献2)引用)

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<sup>\*</sup> Prevention of falls.

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表 1 転倒予防事業の実態調査結果 一「講話」

文 「 料 団 가 肉 尹 未	転倒予防に関する講話					
	1.00 度数 列(%)					
	度数	列 (%)				
開始年度						
1965~1988	3	2.5				
1989~1993	2	1.7				
1994~1998	16	13.3				
1999~2003	99	82.5				
実施期間						
1日	33	26.6				
2 日~1 週間未満	15	12.1				
1 週間~1 か月未満	9	7.3				
1 か月~3 か月未満	12	9.7				
3 か月~6 か月未満	9	7.3				
6 か月~1 年未満	8	6.5				
1 年	30	24.2				
その他	8	6.5				
実施頻度						
ほぼ毎日	2	1.6				
週 2~4 回程度	1	0.8				
週 1 回程度	15	12.3				
月 2~3 回程度	32	26.2				
月1回程度	19	15.6				
2~3 か月に 1 回程度	17	13.9				
その他	36	29.5				
享業評価						
評価している	60	48.0				
評価していない	65	52.0				
継続希望						
継続希望あり	122	97.6				
継続希望なし	3	2.4				
来年度予定						
来年度実施予定あり	117	94.4				
来年度実施予定なし	7	5.6				

転倒予防事業の実態調査2)

# 1. 調査の概要

2000年に実施した転倒予防事業の全国調査3)で、転倒予防事業を実施していると回答した自治体から無作為に抽出した260市町村に調査票を郵送し、回答を求めた(2003年実施).調査票は、前回調査で使用した調査票を改訂したもので、市町村の特性、転倒予防に対する担当者の認識、転倒予防事業の実施状況とその内容、事業(効果)評価の有無とその効果内容、などについて尋ねるものであった.

## 2. 結 果

結果として調査に回答が得られたのは 180 市町

表 2 転倒予防事業の実態調査結果 一「体操」

衣 2 料间 7 奶争未	体操							
	1.0	00						
	度数	列(%)						
開始年度								
1965~1988	6	5.2						
1989~1993	6	5.2						
1994~1998	12	10.4						
1999~2003	91	79.1						
実施期間								
1 🗏	16	13.7						
2 日~1 週間未満	7	6.0						
1 週間~1 か月未満	4	3.4						
1 か月~3 か月未満	17	14.5						
3 か月~6 か月未満	13	11.1						
6 か月~1 年未満	12	10.3						
1 年	40	34.2						
その他	8	6.8						
実施頻度								
ほぼ毎日	3	2.6						
週 2~4 回程度	6	5.2						
週 1 回程度	30	26.1						
月 2~3 回程度	24	20.9						
月1回程度	23	20.0						
2~3 か月に 1 回程度	8	7.0						
その他	21	18.3						
事業評価								
評価している	69	59.0						
評価していない	48	41.0						
継続希望								
継続希望あり	114	97.4						
継続希望なし	3	2.6						
来年度予定								
来年度実施予定あり	111	95.7						
来年度実施予定なし	5	4.3						

村であった(回答率 180/260=69.2%). 95%の市町村が、「高齢者の転倒予防を目的とした保健事業」が重要と考えると回答した. この1年間に該当する事業を実施していた市町村は151(84%)であった(図1).

転倒予防事業の内容では、「転倒予防に関する講話」(84%)と「体操」(79%)が多く、レクリエーションゲーム」、「検診、健康調査」、「筋力トレーニング」がそれに次ぐものであった。いずれの活動も、開始年度は1999~2003年、実施期間は通年、継続希望・次年度予定はありとする市町村が多かった。

実施市町村の多かった「講話」と「体操」に関する結果の詳細を表1,2に示した。実施期間を

表 3 転倒予防事業の実態調査結果 一「筋力トレーニング」

	筋力トレ	ーニング
	1.	00
	度数	列 (%)
開始年度		
1994~1998	6	9.5 j
1999~2003	57	90.5
実施期間		
1日	4	6.2
2日~1週間未満	2	3.1
1 週間~1 か月未満	5	7.7
1 か月~3 か月未満	11	16.9
3 か月~6 か月未満	19	29.2
6 か月~1 年未満	9	13.8
1 年	10	15.4
その他	5	7.7
実施頻度		
ほぼ毎日	3	4.8
週 2~4 回程度	15	23.8
週 1 回程度	14	22.2
月 2~3 回程度	14	22.2
月 1 回程度	7	11.1
2~3 か月に 1 回程度	3	4.8
その他	7	11.1
事業評価		
評価している	52	81.3
評価していない	12	18.8
継続希望		
継続希望あり	62	95.4
継続希望なし	3	4.6
実施予定		
来年度実施予定あり	60	93.8
来年度実施予定なし	4	6.3

1年と回答した市町村のなかには、1年間の事業計画の一つという意味で回答した所が少なからず含まれていた. したがって、「講話」は、年に1回のみ実施という市町村が最多と考えられた.また、講話を含む事業を一定期間継続する市町村では、1月に2、3回の頻度で実施する所が多かった.「体操」については、年に1回も少なくなかったが、1か月~3か月を筆頭に、一定の期間実施する市町村が多く、頻度としては、週に1回から月に1回まで、ある程度定期的に実施している傾向がみられた.

参考までに、改正された介護保険制度のなかで、 予防介護サービスとしての注目度が高い「筋力ト レーニング」についての結果も示す(表3). 開始 時期は遅い、実施期間は3か月~6か月が最多、 体操よりも高頻度で実施されている、などの傾向 がみられた。

なお,転倒予防事業に携わるスタッフについては,保健師が中心であり,97%以上の市町村で保健師が担当スタッフに含まれていた.理学療法士(PT)/作業療法士(OT),栄養士,健康運動指導士が担当者に含まれる市町村は約6割だが,医師が含まれる所は約1/4であった.

事業の評価については、105 市町村(69.5%)が何らかの評価をしていると回答した。また、効果評価をする市町村の約 60%が「講話」と「筋力トレーニング」を、約 50%が「体操」と「歩き方教室」を有効としていた(図 2).

#### 3. まとめ

結論として、市町村の実施する転倒予防事業の内容としては、「講話」と「体操」が圧倒的に多かった。やはり、「転倒に関する話」と「身体を動かす体操」の組み合わせが転倒予防教室の定番と考えられる。さらに、自己申告的な要素の強い結果だが、「講話」と「体操」は、効果もあるとする市町村が多かった。この2つの活動が、実施可能性が高く、なおかつ、実施主体である自治体もある程度の評価をしているということになるであろう。

# 転倒予防事業の効果について4)

#### 1. 研究の概要

地域における転倒予防を目的とした介入プログラムの効果については、これまでにも研究がなされており、運動を中心としたプログラムに転倒予防効果があったとする報告がある<sup>5,6)</sup>. われわれは、日本で一般的に実施されている転倒予防事業の効果を検討するために、前述の実態調査で実施市町村の多かった「講話」と「体操」を組み合わせたプログラムを、やはり回答の多かった実施期間である約2か月間行い、その効果を検討した.

具体的には愛知県豊田市若林地区で,65歳以上の在宅高齢者から参加者を募集し,転倒予防教室を実施した.教室は,1回2時間で,2週間に1回のペースで計5回実施した.教室の前半には,転倒予防と関連する講話を行った.これにより,プ

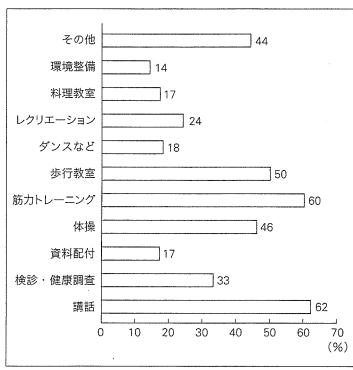


図 2 転倒予防事業の効果

各活動を実施し、さらに、効果評価もしていると回答した市町村数を分母とした場合の、効果ありとした市町村の割合(文献<sup>2)</sup>引用)

ログラム参加への動機付けを行うとともに,運動や転倒予防に関する参加者の知識の向上を図った.教室の後半では,筋力・持久力に有用とされる各種運動実践(ストレッチ,下肢・体幹を中心とした筋力トレーニング,リズム体操,歩行訓練)を行った.初回および最終回の教室の前半では,質問紙調査と体力測定を行い,転倒ならびに心身機能に関する指標を得た.

また,同地区の老人会の協力を得て,同じく 65歳以上の高齢者に対照群を設定し,心身機能の変化について,教室参加者との比較分析を行った.

#### 2. 結果

転倒経験と転倒恐怖感の比率の変化を,転倒予防教室参加群と対照群で比較し,直接的な転倒予防効果を検討した.結果としては,両群に差がなく,今回の教室の転倒予防に対する直接的な介入効果は確認できなかった(表 4).ただし,今回は,教室終了後の転倒発生状況は検討していない.教室実施後の転倒について追跡調査を行い,その予防効果を検討することにより,異なる結果が得られた可能性はあるだろう.

表 4 転倒経験と転倒恐怖感に対する効果 転倒経験

第 1 回測定 (過去 1 年 間の転倒)	第 2 回測定 (第 1 回測 定後の転倒)	介入群(人)	対照群(人)
あり	あり	1	0
あり	なし	6	4
なし	あり	1	1
なし	なし	9	10
n <sub>.</sub>		17	15

(z=-0.48, ns)

#### 転倒恐怖感

第 1 回測定	第2回測定	介入群 (人)	対照群 (人)
あり	あり	11	3
あり	なし	3	4
なし	あり	1	4
なし	なし	2	4
n		17	15

(z=-0.53, ns)

次に、心身機能〔握力、開眼片足立ち、最大歩幅、10 M 歩行歩数(普通歩および速歩)〕、転倒セルフエフィカシー(日常的な活動に対する自信の程度)、抑うつに対する教室の介入効果を、性、年齢、教育年数、入院歴、活動能力を調整して検討した。

その結果,介入群のみに統計学的に有意な転倒 セルフエフィカシー得点の上昇および抑うつ得点 の減少が認められ,心理機能に関する有意な介入 効果が示された.

# 3. まとめ

市町村の転倒予防事業として一般的と考えられる内容の転倒予防教室を行い、その効果を検討した. 転倒率や転倒恐怖感、あるいは各種身体機能に対する効果を確認することはできなかったが、心理機能すなわち転倒セルフエフィカシーや抑うつ症状の改善に有用である可能性が示された. 費用対効果なども検討しなければ最終的な結論は出せないが、心理機能に対する有意な効果があったことを考えると、今回のような期間の限定された転倒予防教室にも、十分に実施意義はあると考え

られる.

なお、短期間の介入では、転倒予防に重要な筋力などの運動機能に十分な効果がみられないとする報告はこれまでにもあることから<sup>7)</sup>、身体機能に有意な効果をもたらすには、今回の教室よりは長期のものが望ましいと考えられる。しかし、市町村などにおける事業として実施する場合には、ある程度期間が限定されてしまうことが避けがたい場合もある。そのときは、教室終了後に参加者が運動や勉強を継続できる工夫が重要となるだろう。

# おわりに

最初にも述べたが、本稿の結果は、介護保険法 改正前のものである。介護予防サービスとして転 倒予防教室が実施可能となり、転倒予防事業は一 層普及し、内容も豊富になり、効果の検証も進む と考えられる。転倒予防事業の変遷について、今 後さらに注目する必要があるだろう.

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# - News-

鹿児島県内を含め、全国の授産施設で働く障害者から「働くほど負担増になる」など批判が噴出していた4月施行の障害者自立支援法.国は見直しを決め、県を通して各市町村への説明を進めている.早々の見直しに福祉行政への不信の声もあるが、「希望が見えてきた」と喜ぶ関係者が多い.

同法の施行により、施設内での作業による工賃から利用料を引かれると、手取りはゼロに近くなる障害者もいた.

見直しでは、工賃の月額が4万円以下の場合、施設利用料の負担を少なくした。厚生労働省社会・援護局の障害保健福祉部によると、食費などの負担額を支払っても、手元には少なくとも年間28万8,000円は残る計算だという。

同部は「障害者の働くことへのインセンティブ(誘因,刺激)を高め、より一層の配慮をする観点から今回の見直しとなった」としている.

厚労省は5月末に事務連絡の形で鹿児島県に見直

# 障害者自立支援法,施設利用料見直し 10月から、厚労省

しを通知.6月末にあった同省の障害保健福祉関係主管課長会議で具体的な数値を示した.県は7月中旬に見直しの内容を市町村に説明したほか,今月末にも説明会を開く.10月から実施予定だ.

県内の施設関係者は、制度の行方を慎重に見守る.

日置市の重度身体障害者授産施設「鹿児島太陽の 里」の佐多京子理事長は「施行前から問題点が見え ていたので、見直しが遅れたのは残念. ただ大勢の 障害者が恩恵を受けることになり、希望が見えてき た. 今後も利用者の生の声を訴えていきたい」と話 している.

始良町の身体障害者通所授産施設サン・ヴィレッジ始良の山之内浩子施設長は障害者の働きがいが考慮されたことを評価.一方で、「生活全般にわたる1割負担が重圧で、まだまだ暮らしにゆとりがない」と話している.

(南日本新聞・鹿児島 2006年8月16日)

#### ORIGINAL ARTICLE

# Effect of regular exercise on homocysteine concentrations: the HERITAGE Family Study

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Abstract We investigated whether regular aerobic exercise could affect plasma total homocysteine (tHcy), and whether there were sex-related or racial differences in tHcy changes. Data were available for 816 black and white men and women, aged 17–65 years, 711 of whom completed a 20 week aerobic exercise training program. The tHcy concentration was measured in frozen plasma samples by an HPLC

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method. In Blacks, tHcy did not change with exercise training [men -0.5 (SD 3.7)  $\mu$ mol/l, women 0.0 (2.2) µmol/l) but increased significantly in Whites (men +0.3 (1.7)  $\mu$ mol/l, women +0.2 (1.6)  $\mu$ mol/l). No sex-related differences were found in either racial group. Changes in tHcy correlated negatively with baseline homocysteine (r = -0.40, P < 0.0001). Homocysteine levels of the "High" (hyperhomocysteinemia) ( $\geq 15 \, \mu \text{mol/l}$ ) group (n = 30) decreased significantly with regular aerobic exercise from 23.1 (12.1) to 19.6 (7.6) µmol/l. Homocysteine levels of the "Normal" group increased slightly from  $8.2 \pm 2.2$  to  $8.5 \pm 2.4 \,\mu$ mol/l. Men exhibit racial differences for tHcy responses to exercise training. Regular aerobic exercise has favorable effects on individuals with hyperhomocysteinemia, but tHcy slightly increased in individuals within the normal range.

**Keywords** Aerobic exercise training · Sex · Homocysteine · Hyperhomocysteinemia · Racial differences

## Introduction

Elevated plasma total homocysteine concentrations (tHcy) are thought to contribute to atherosclerosis and thrombosis in several ways: (a) endothelial cell injury and endothelial dysfunction, (b) increased vascular smooth muscle cell growth, (c) increased platelet adhesiveness, (d) enhanced low density lipoprotein oxidation and deposition in the arterial wall, and (e) direct activation of the coagulation cascade (Fonseca et al. 1999). Epidemiological studies have shown that elevated tHcy are independently associated with an

increased risk of coronary artery disease (Langman et al. 2000; Ridker et al. 1999). Further, several observational studies have found that lowering tHcy was associated with reduced incidence of heart attack and strokes (Homocysteine Studies Collaboration 2002; Boushey et al. 1995; Schnyder et al. 2001).

Little information is available on the effect of exercise on tHcy. Although a few studies on endurance trained men (Konig et al. 2003) and untrained young women (De Cree et al. 1999) have shown that a single bout of intensive exercise acutely increased tHcy, long-term (6 months) regular exercise may be associated with a reduction in tHcy in young overweight and obese women (Randeva et al. 2002). These studies were, however, too small to provide conclusive evidence for an effect of regular exercise on tHcy.

An epidemiological study (Ganji and Kafai 2003) showed that both sex and race were important predictors of tHcy. The difference in tHcy between men and women was explained by alcohol consumption and blood concentrations of folate, vitamin B<sub>12</sub> (cyanocobalamin), creatinine and cotinine. On the other hand, racial differences are thought to be partly accounted for variation in allele frequency at the methylenetetrahydrofolate reductase gene (Cappuccio et al. 2002). To our knowledge, no data have been reported on race or sex differences for the changes in tHcy in response to exercise training. Therefore, the purpose of this study was to investigate the effects of relatively long-term regular exercise on tHcy in a large sample of black and white men and women.

#### Methods

#### Subjects

The HERITAGE Family Study was designed to define the role of the genotype in cardiovascular, metabolic and hormonal responses to aerobic exercise training. The aim, design and measurement protocol of the HERITAGE Family Study has been previously described in details elsewhere (Bouchard et al. 1995).

The present study is based on baseline data from 816 sedentary subjects, who were recruited and studied at four clinical centers. They came from families that included parents (aged  ${\leq}65$  years) and adult offspring (aged  ${\geq}17$  years). They were required to be sedentary at baseline, with a body mass index (BMI) <40 kg/m² (a few cases with BMI  ${\geq}40$  kg/m² were included with sufficient clinical justification), resting systolic blood pressure <160 mm Hg, resting diastolic blood pressure <100 mm Hg, plasma total cholesterol <350 mg/dl, and

fasting plasma triglycerides <500 mg/dl. Subjects who had renal, hepatic or cardiac disease, were diabetic, or had hypothyroidism, or were being treated with lipid-lowering, hypertensive or hypoglycemic drugs were excluded. The study relies also on data from the response to a 20 week aerobic exercise training program in 730 subjects (90 black men, 159 black women including 18 post-menopausal and 46 who were taking hormones, 236 white men, and 245 white women including 45 post-menopausal and 105 who were taking hormones). The study protocol was approved by the Institutional Review Board at each clinical center. The aim and design of the study were explained to all subjects before they gave written informed consent.

#### Measures

Body weight, height, waist and hip circumferences were measured according to standardized procedures (Wilmore et al. 1997), and BMI was calculated as body weight (kg) divided by height (m<sup>2</sup>). Body composition (fat mass and fat free mass) was estimated using the hydrostatic weighing technique. Details of the protocol of the hydrostatic weighing technique and body composition estimation are provided elsewhere (Wilmore et al. 1997).

Resting BP was measured using Colin STBP-780 automated units before 11 AM in the post-absorptive state (Rankinen et al. 2000). Subjects were asked to abstain from caffeine-containing or tobacco products for 2 h before measurements were made. Subjects rested for 5 min before the initial measurement. Blood samples were obtained after a 12 h fast. Cholesterol was determined in plasma by enzymatic methods (Despres et al. 2000).

The tHcy (the sum of homocysteine, homocystine, and homocysteine-cysteine mixed disulfides, free and protein bound) were measured in frozen plasma samples (-70°C) by an HPLC method (Durand et al. 1996). The intra- and inter-assay coefficients of variation for tHcy are 3.0% (n = 12) and 3.3% (n = 50), respectively. Plasma folate and vitamin B<sub>12</sub> concentrations were determined by means of radioimmunoassay using a commercial kit (SimulTRAC-SNB\_B<sub>12</sub>/Folate, ICN Diagnostics, Orangeburg, NY). The intra- and inter-assay coefficients of variation are 6.3% (n = 20) and 10.3% (n = 14), respectively, for foliate, and 4.9% (n = 20) and 4.3% (n = 14), respectively, for vitamin B<sub>12</sub>. Plasma vitamin B<sub>6</sub> (pyridoxal phosphate) concentrations were also determined by means of a radioimmunoassay using a commercial kit (Vitamin B<sub>6</sub> (<sup>3</sup>H) REA, American Laboratory Products Company, Windham, NH). The intra- and inter-assay coefficients



of variation for vitamin  $B_6$  are 4.6% (n = 9) and 10.2% (n = 8), respectively.

Progressive maximal exercise tests to exhaustion were conducted both before and after the exercise training program on a stationary cycle ergometer (Ergo-Metrics 800S, SensorMedics, Yorba Linda, CA) connected to a SensorMedics 2900 metabolic cart.

#### Exercise training protocols

Each subject was trained three sessions per week for 20 weeks on stationary cycle ergometers that were computer controlled to automatically maintain the participant's target heart rates corresponding to heart rates associated with fixed percentages of the baseline  $VO_{2\max}$  test (Skinner et al. 2000). The intensity and duration of the training program was adjusted each 2 weeks. Training began at a heart rate corresponding to 55% of each subject's baseline  $VO_{2\max}$  for 30 min per session and progressed to an intensity of 75% for 50 min during the last 6 weeks. All training sessions were supervised on site.

Subjects were asked not to change their eating patterns (meals and supplement use) during the intervention period.

#### Statistical analysis

General linear model analyses were used to test for differences between men and women as well as between the two ethnic groups. Paired *t*-tests were used to assess differences between variables before and after the exercise training program. Multiple regression analyses with the forward stepwise method were performed to estimate the independent contributions of age, sex, race, menopausal status, taking hormones,

BMI, waist circumference, body composition,  $VO_{2max}$ , resting blood pressure, plasma levels of cholesterol, folate, vitamin  $B_6$  and vitamin  $B_{12}$  to the variations in tHcy at baseline and changes in tHcy in response to aerobic exercise training. The relationship between two measurements was assessed by Pearson and Spearman rank correlation coefficients. Based on a position statement of the American Heart Association, we classified subjects into two groups: subjects with tHcy in the normal range (<15  $\mu$ mol/l, "Normal" group) and subjects with elevated levels or hyperhomocysteinemia ( $\geq$ 15  $\mu$ mol/l, "High" group) (Malinow et al. 1999). Probability values below 0.05 were regarded as significant. The data were analyzed with the Statistical Analysis System (SAS), version 9.1.

#### Results

Physical and biochemical characteristics of subjects at baseline are presented in Table 1 (n = 816). Detailed values of anthropometric and body composition measurements (Wilmore et al. 1997), resting blood pressure (Rankinen et al. 2000), and plasma lipids (Despres et al. 2000) were presented in previous reports. The tHcy levels were higher in men in both ethnic groups, and were higher in Blacks in both sexes.

For the whole sample (n=711), the mean change in tHcy was only +0.1 µmol/l from baseline ( $8.8\pm4.4~\mu mol/l$ ) to post-exercise training ( $8.9\pm3.6~\mu mol/l$ ) (P=0.096). Table 2 shows that tHcy did not change in Blacks but increased significantly in Whites. Vitamin B<sub>6</sub> remained unchanged, whereas vitamin B12 decreased significantly in all groups. Folate increased significantly in black men only. When the changes were compared between the two ethnic groups, we found a

Table 1 Comparison of baseline data between men and women, and between Blacks and Whites

	Blacks		Whites		Race difference		
	Women (n = 191)	Men (n = 111)	Women (n = 260)	Men (n = 254)	Women	Men	
Age (years)	33.0 (11.4)	32.9 (12.3)	35.1 (14.1)	36.2 (14.9)	0.089	0.028	
Height (m)	1.62 (6.6)	1.76 (6.7) <sup>á</sup>	1.64 (6.4)	$1.78 (6.3)^{\acute{a}}$	0.041	0.01	
Weight (kg)	74.4 (17.9)	84.6 (18.6) <sup>a</sup>	67.2 (13.6)	84.4 (16.2) <sup>a</sup>	< 0.0001	0.907	
BMI (kg/m²)	28.2 (6.5)	27.4 (5.6)	25.1 (5.0)	26.7 (4.9) <sup>á</sup>	< 0.0001	0.218	
Homocysteine (µmol/l)	8.5 (4.2)	$11.0\ (7.2)^a$	7.7 (2.7)	9.4 (3.7) <sup>á</sup>	0.01	0.004	
Folate (nmol/l)	12.0 (8.3)	12.0 (8.5)	16.6 (15.0)	14.1 (10.3)	0.001	0.034	
Vitamin B <sub>6</sub> (nmol/l)	40.6 (38.0)	64.9 (59.4)	56.2 (63.0)	60.9 (51.9) <sup>a</sup>	0.0001	0.763	
Vitamin B <sub>12</sub> (nmol/l)	332 (153)	328 (183)	286 (144)	289 (112)	0.0004	0.099	
VO <sub>2max</sub> (ml/min)	1,753 (365)	2,758 (490)a	1,912 (347)	3,026 (582) <sup>a</sup>	< 0.0001	< 0.0001	

Data are expressed as mean (SD)

BMI body mass index, VO<sub>2max</sub> maximal oxygen uptake

<sup>&</sup>lt;sup>a</sup> P < 0.001 significantly different from women



Table 2 Comparison of changes in measurements between men and women, and between Blacks and Whites

	Blacks		Whites		Race difference		
	Women (n = 151)	Men (n = 87)	Women (n = 243)	Men (n = 230)	Women P-value	Men P-value	
Weight (kg)	-0.4 (2.9) <sup>a</sup>	-0.8 (3,1) <sup>a</sup>	-0.1 (2.1)	-0.3 (2.1) <sup>a</sup>	0.224	0.252	
BMI (kg/m <sup>2</sup> )	-0.2(1.1)	$-0.2(0.9)^{a}$	-0.0(0.8)	$-0.1 (0.7)^{a}$	0.279	0.376	
Homocysteine (µmol/l)	+0.0 (2.3)	-0.5 (3.8)	$+0.2(1.6)^{a}$	$+0.3(1.7)^a$	0.407	0.04	
Folate (nmol/l)	+0.9 (9.6)	$+2.8(7.9)^a$	-0.7(9.0)	-0.3(6.9)	0.111	0.003	
Vitamin B <sub>6</sub> (nmol/l)	+3.3 (27.6)	+12.2 (76.2)	-1.5(62.2)	+6.6 (64.7)	0.299	0.521	
Vitamin B <sub>12</sub> (nmol/l)	$-17(71)^{a}$	$-14(79)^{a}$	$-23 (62)^a$	$-18(68)^{a}$	0.404	0.306	
VO <sub>2max</sub> (ml/min)	+336 (151) <sup>a</sup>	+411 (201) <sup>a, b</sup>	+349 (183)ª	+450 (236) <sup>a, b</sup>	0.447	0.185	

Data are expressed as mean (SD)

BMI body mass index,  $VO_{2max}$  = maximal oxygen uptake

significant difference in males for folate and homocysteine. No sex difference was found for any of the variables. After exercise training, the mean (SD) values of tHcy were 8.6 (3.4)  $\mu$ mol/l for black women, 10.8 (5.4)  $\mu$ mol/l for black men, 8.0 (2.4)  $\mu$ mol/l for white women, and 9.6 (3.4)  $\mu$ mol/l for white men. Sex and racial differences were identical to those at baseline.

We quantified the independent contributions of the variables considered here to the variance in tHcy. At baseline (Table 3), folate was the best predictor of tHcy in both sexes, and both races. Age, ethnicity and vitamin  $B_{12}$  were also significant predictors of tHcy. When exercise training induced changes in tHcy were used as the dependent variable, baseline homocysteine levels, and changes in folate were the strongest predictors in the whole sample as well as in the sex and race subgroups (Table 3). Although  $VO_{2max}$  was not selected as a significant predictor, increases in  $VO_{2max}$  tended to associate with decreases in tHcy (P = 0.06) in the whole sample.

Figure 1 illustrates the relationship between baseline tHcy and change in tHcy in response to exercise training. Changes in tHcy were negatively correlated with baseline tHcy (Pearson correlation coefficient = -0.40, P < 0.0001 and Spearman rank correlation coefficient = -0.25, P < 0.0001).

Figure 2 displays individual tHcy data for the High group (n=30) at baseline and after training. Mean values of tHcy decreased from 23.1 (SD 12.1)  $\mu$ mol/l to 19.6 (7.6)  $\mu$ mol/l (P=0.01). After training, 21 (70%) individuals (3 black women, 9 black men, 3 white women, and 6 white men) decreased their tHcy. Eight of the 21 individuals decreased their tHcy to less than 15  $\mu$ mol/l. On the other hand, in the Normal group (n=681), only 8 (1%) individuals (2 black women, 3 black men, 1 white women, and 2 white men) increased their tHcy to more than 15  $\mu$ mol/l. The Normal group

had a statistically significant increase in tHcy from 8.2 (2.2)  $\mu$ mol/l to 8.5 (2.4)  $\mu$ mol/l (P < 0.0001).

Figure 3 compares tHcy changes between the Normal and High groups. A significant (P < 0.0001) difference was observed between the Normal [+0.3 (1.5) µmol/l] and High [-3.5 (7.0) µmol/l] groups for the tHcy response to exercise training. The difference was still found after adjustment for age, sex, race and baseline tHcy (P = 0.0028). Folate levels increased significantly (+1.1 ± 3.0 nmol/l, P < 0.05) during the exercise training in the High group but remained unchanged in the Normal group. Vitamin  $B_{12}$  levels did not change in the High group but decreased significantly (-16.5 ± 97.8 pmol/l, P < 0.0001) in the Normal group.

#### Discussion

We found that the 20 week aerobic exercise training program reduced significantly tHcy (-3.5 µmol/l, P = 0.01) in those with elevated tHcy at baseline. Moreover, a significant difference in tHcy changes remained between the Normal and High groups even after adjustment for age, sex, race and baseline tHcy (P = 0.0028). Boushey et al. (1995) have reported that about 10% of the population's coronary artery disease risk was attributable to tHcy, and Ueland et al. (2000) found that an increase of 5 µmol/l in tHcy could be associated with a 20% increased risk of cardiovascular disease. Schnyder et al. (2001) found that lowering tHey from 11.1 to 7.2 µmol/l reduced significantly the rate of coronary restenosis after angioplasty and decreased the incidence of major adverse cardiac events. In a more recent study, lowering tHcy by 25% (3 μmol/l) was associated with an 11% lower ischemic heart disease and 19% lower stroke risk (Homocysteine



<sup>&</sup>lt;sup>a</sup> Training response (post–pre) P < 0.05

<sup>&</sup>lt;sup>b</sup> P < 0.01 significantly different from women

Table 3 Results of multiple regression analysis

Independent	Homoc	ysteine	at baseline			Independent	Homocys	steine	training re	sponse	
variable	Beta	F	P	Partial R <sup>2</sup>	Model R <sup>2</sup>	variable	Beta	F	P	Partial R <sup>2</sup>	Model R <sup>2</sup>
[All]											
Folate	-0.18	118.1	< 0.0001	14.2	14.2	B_homocysteine	-5.36	72.8	< 0.0001	10.5	10.5
Sex <sup>a</sup>	-0.1	77.4	< 0.0001	8.4	22.6	ΔFolate	-0.04	21.5	< 0.0001	3.0	13.5
Age	0.002	73.8	< 0.0001	7.3	29.9	Age	0.02	7.9	0.005	1.1	14.6
B <sub>12</sub>	-0.17	44.9	< 0.0001	4.2	34.1	B_folate	-0.78	8.9	0.003	1.2	15.8
Raceb	-0.04	18.6	< 0.0001	1.7	35.8	$B_VO_{2max}$	0.0004	11.4	0.0008	1.5	17.3
						ΔB12	-0.002	4.5	0.036	0.6	17.9
						B_B6	-0.004	4.4	0.036	0.6	18.5
[Male]											
Folate	-0.23	65.6	< 0.0001	16.7	16.7	B_homocysteine	-5.9	44.4	< 0.0001	13.4	13.4
Age	0.002	48.3	< 0.0001	10.8	27.5	ΔFolate	-0.05	15.3	0.0001	4.4	17.8
B <sub>12</sub>	-0.16	14.6	0.0002	3.1	30.6	ΔB12	-0.004	5.7	0.018	1.6	19.4
Race	-0.05	13.4	0.0003	2.8	33.4	Age	0.03	4.1	0.044	1.2	20.6
Fat%	0.002	8.6	0.004	1.7	35.1	$B_VO_{2max}$	0.0006	5.9	0.015	1.6	22.2
						B_folate	-0.9	5.1	0.025	1.4	23.6
[Female]											
Folate	-0.15	60.3	< 0.0001	13.6	13.6	B_homocysteine	-4.61	32.2	< 0.0001	8.9	8.9
B <sub>12</sub>	-0.18	35.9	< 0.0001	7.4	21.0	ΔFolate	-0.03	8.9	0.003	2.4	11.3
Age	0.002	22.1	< 0.0001	4.3	25.3	B_B6	-0.84	6.2	0.013	1.6	12.9
Race	-0.03	6.8	0.009	1.3	26.6	ΔΒ6	-0.003	4.9	0.028	1.3	14.2
						Age	0.02	5.3	0.021	1.4	15.6
[Blacks]											
Folate	-0.26	50.9	< 0.0001	17.4	17.4	B_homocysteine	-8.0	61.0	< 0.0001	25.0	25.0
Sex	-0.17	34.3	0.0001	10.3	27.7	ΔFolate	-0.05	8.4	0.004	3.3	28.3
Age	0.002	21.9	0.0027	6.0	33.7	ΔΒ6	-0.006	5.4	0.021	2.1	30.4
B <sub>12</sub>	-0.17	14.6	0.0096	3.8	37.5						
Cholesterol	0.02	4.2	0.041	1.1	38.6						
[Whites]											
Folate	-0.16	66.2	< 0.0001	12.4	12.4	B_homocysteine	-0.03	42.0	< 0.0001	8.8	8.8
Age	0.002	61.3	< 0.0001	10.2	22.6	ΔFolate	*	10.2	0.0015	2.1	10.9
Sex	-0.07	45.0	< 0.0001	6.8	29.4	Sex		9.2	0.0026	1.8	12.7
B <sub>12</sub>	-0.17	42.2	< 0.0001	5.9	35.3	B_B6		9.8	0.0019	1.9	14.6
Resting DBP	0.002	7.0	0.008	1.0	36.2	B_folate		6.8	0.009	1.3	16.0
						Age		12.1	0.0006	2.3	18.3
						ΔB6		4.4	0.036	0.8	19.1

a 1 = men, 2 = women

Studies Collaboration 2002). Therefore, our observation that tHcy can be lowered by regular exercise in those with high levels is coherent with a number of studies indicating that it may reduce significantly the risk of events in individuals with hyperhomocysteinemia.

#### Sex difference

The tHcy concentrations are known to be higher in men than in women (Ganji and Kafai 2003; Carmel et al. 1999; Fukagawa et al. 2000; Lussier-Cacan et al. 1996; Morris et al. 2000; Nygard et al. 1995). Ganji et al. (2003) and Carmel et al. (1999) found that the sex-related difference could be explained by alcohol consumption, and concentrations of plasma folate, vitamin  $B_{12}$ , creatinine and cotinine. Folic acid and vitamin  $B_{12}$  are involved as co-factors in metabolic

pathways catalyzed by the enzymes 16,2methylenetetrahydrofolate reductase and methionine synthase, respectively, whereas vitamin B<sub>6</sub> is a cofactor for cystathionine beta synthase (Kang et al. 1992). A number of studies have shown inverse relationships of tHcy with plasma/serum levels of folate, vitamin B<sub>6</sub> and vitamin B<sub>12</sub> (Robinson et al. 1998; Selhub et al. 1993). Moreover, differences in rates of homocysteine remethylation (Fukagawa et al. 2000) and estrogen concentrations (Morris et al. 2000) may also contribute to the homocysteine sex dimorphism. Remethylation is one of the major pathways for homocysteine metabolism. In remethylation, homocysteine is salvaged by acquisition of a methyl group from N5-methyl-tetrahydrofolate in a vitamin B<sub>12</sub> dependent pathway or from betaine in a pathway occurring primarily in the liver (McKeever et al. 1991). Fukagawa et al. (2000) and



b 1 = blacks, 2 = whites

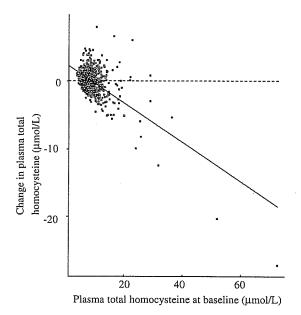
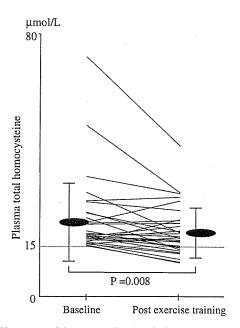


Fig. 1 Association between baseline homocysteine and regular exercise-induced changes in homocysteine. Pearson correlation coefficient = -0.40 (P < 0.0001), Spearman correlation coefficient = -0.25 (P < 0.0001)



**Fig. 2** Plasma total homocysteine levels in the High group at baseline and post-exercise training. *Vertical lines* indicate means (filled circle) and SD

McKeever et al. (1991) found that the remethylation rate was significantly higher in women than in men. They concluded that the sex-related difference is partially explained by homocysteine remethylation rates. Morris et al. (2000) found that higher estrogen concentrations

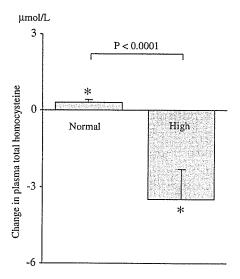


Fig. 3 Comparison of changes in plasma homocysteine levels between the "Normal" and "High" groups. Data are expressed as means  $\pm$  SEM. \*P < 0.01, within group difference (pre vs post)

are associated with lower tHcy, independent of nutritional status and muscle mass.

In the Hordaland Homocysteine Study (Nygard et al. 1995), tHcy levels were 19% higher in men (10.8  $\mu mol/l$ ) than in women (9.1  $\mu mol/l$ ) in middle age participants but only 11% (men 12.3  $\mu mol/l$  and women 11.0  $\mu mol/l$ ) in elderly subjects. Although our data also indicated that baseline tHcy was higher in men than in women, there was no difference in exercise-induced changes in tHcy between men and women.

#### Racial differences

Several studies (Carmel et al. 1999; Ganji and Kafai 2003; Morris et al. 2000) have reported that Whites have 7–8% higher tHcy than Blacks. For instance, Ganji and Kafai (2003) found that tHcy was 8% higher in Whites (10.4  $\mu$ mol/l) than in Blacks (9.6  $\mu$ mol/l). Carmel et al. (1999) speculated that the higher tHcy in Whites might be explained by their lower vitamin B<sub>12</sub> status compared with Blacks. On the other hand, the third National Health and Nutrition Survey in the United States (Jacques et al. 1999) found no racial difference in tHcy.

The present study indicates that baseline homocysteine levels were higher in Blacks than in Whites, and differences were also found for the training changes in homocysteine levels between Black and White men. Several investigators have reported that folate and vitamin  $B_{12}$  were predictors of blood homocysteine concentrations (Koehler et al. 2001; Morris et al. 2000).



Using multiple regression analyses, folate was found to be the strongest predictor of homocysteine in the present study. Our results also showed that folate levels were higher in Whites than in Blacks although vitamin  $B_{12}$  levels were higher in Blacks.

The present study has some limitations. First, since the primary goal of the HERITAGE Family Study is to study the role of genotype in the responsiveness to regular exercise, a control group was not deemed necessary. Second, subjects were asked not to change their eating patterns during the 20 week intervention period, but we have no direct assessments of folic acid, vitamin  $B_6$  and  $B_{12}$  intakes over the duration of the exercise protocol.

In summary, we have examined the effects of exercise training on tHcy concentrations in both sexes and in Blacks and Whites. Baseline tHcy is higher in men than in women, consistent with previous studies. However, no difference between men and women was found for the changes in tHcy levels as a result of regular exercise. Baseline tHcy was higher in Blacks than in Whites, and in men, differences were also found for the changes in tHcy between the two ethnic groups. Twenty weeks of regular exercise reduced tHcy in individuals with baseline hyperhomocysteinemia, although tHcy slightly increased in individuals who were in the normal range of tHcy at baseline.

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# A novel exercise for improving lower-extremity functional fitness in the elderly

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ABSTRACT. Background and aims: Many falls in the elderly are caused by tripping. After tripping, a certain level of lower-extremity functional fitness is necessary, in order to make protective responses and to avoid falling. The purpose of this study was to test whether our new exercise program (a square-stepping exercise: SSE) would improve lower-extremity functional fitness in the elderly. Methods: Fifty-two individuals aged 60-80 years were divided into two groups (non-randomized control design); SSE (n=26) and controls (n=26). Lower-extremity functional fitness was defined as standing up from a lying position (agility), chair-stand in ten seconds (leg power), walking round two cones (locomotion speed), sit-and-reach (flexibility) and single-leg balance with eyes closed (balance). The SSE group participated in a six-month regimen of SSE once a week. SSE was performed on a thin mat of 250 cm by 100 cm, partitioned into 40 small squares (25 cm each side). SSE included not only forward steps but also backward, lateral and oblique steps, and step patterns were progressively made more complicated. Controls maintained their usual lifestyles. Results: In the SSE group, significant improvements were observed in agility, leg power, locomotion speed, flexibility and balance. No significant changes were detected in any tests in the control group. Conclusions: The SSE program improved lower-extremity functional fitness, lack of which constitutes a risk factor for falls in the elderly. This program should be tested further to determine if it can effectively reduce the incidence of falls in the elderly. (Aging Clin Exp Res 2006; 18: 242-248)

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#### INTRODUCTION

In Japan, a national survey found the incidence (per 10,000 per year) of hip fracture in 1997 was 17.3 (men) and 40.8 (women) in persons 60-69 years old, and

57.4 (men) and 147.8 (women) in those 70-79 years old (1). Falls are the most common cause of hip fractures, leading to decreased mobility, restriction to bed, and/or death; in addition, not only hip fractures but also minor injuries such as joint dislocation, lacerations and bruises are also caused by falls (2). As well as fall-associated injuries, falls may lead to an increased fear of falling which can restrict social activities, thereby decreasing independence and overall quality of life.

An interview-based community survey (3) reported that 35% of older residents had suffered one or more falls in the preceding year, and that 53% of the falls had been caused by tripping. Other causes, much less common, were dizziness (7.8%), black-out (6.4%) or accident (5.2%). For many elderly people, impact velocities at the ground after tripping were within one standard deviation of the estimate of the mean impact velocity needed to fracture a femur (4). Falling sideways, which is often observed after slipping, is also associated with the incidence of hip fractures (4, 5); the impact velocity after slipping also reaches the estimated femur fracture velocity (4). Therefore, the prevention of falls caused by elderly persons tripping or slipping is one of the most important areas for maintaining independence and quality of life in this age group.

Effective interventions for preventing falls should include quick stepping in any direction and the generation of enough force at push off to support the whole body following a trip or slip (6). Quickness (reaction speed/agility) and power in the lower extremity, which have been implicated as factors influencing falls, decrease with age (2, 7-10). In most elderly people, the ability to respond quickly and forcefully may be impaired, leading directly to falling. To the best of our knowledge, there are few studies concerning the development of an intervention program to improve speed and power in the lower extremities of the elderly. This study aimed at developing a novel exercise program for improving lower-extremity

Key words: Fall, risk, slip, square-stepping exercise, trip.

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functional fitness in the elderly, and to assess its effects on fall-related risk factors.

### **METHODS**

Study design

An age- and gender-matched, six-month intervention and non-randomized control trial was conducted in Gifu, the capital city of Gifu Prefecture, located in the centre of Japan.

### Participants

Participants in the exercise group were recruited in two ways. One was by direct mailing to pensioners who had an account in the Juroku Bank (Gifu, Japan). Approximately 38,000 letters were sent to people who lived in the area around the building in which the exercise program was conducted. Another procedure was to use leaflets, which were placed in the main office and 60 branch offices of Juroku Bank in Gifu Prefecture. The mailer or leaflet, besides our program, also contained information on several free-of-charge culture classes for the elderly, such as Chinese conversation and "shogi" (Japanese chess) classes. Persons receiving the mailer or leaflet could attend and choose any class from the list, including our program.

Twenty-six people aged 60-80 years agreed to participate in the study (6 men, 20 women). To lower the risks of accident by exercise, five consecutive low-intensity exercise sessions (60 minutes each) over a period of 10 weeks were given to participants before the study. These exercise sessions mainly consisted of stretching the lower extremities while sitting or lying on a mat, and calisthenics for the upper extremities while in a standing position. Participants then engaged in the pre-test and square stepping exercise (SSE) program (see below) for six months without interruption, but were not encouraged to engage in any other new forms of exercise. Once an exercise group was identified, age- (±3 years) and gender-matched controls were selected at random from among cohort members of another surveillance program, in which elderly individuals aged 60 or more living in the city attended as participants of another research program focused on aging and lifestyle. Controls were asked to maintain their lifestyles for six months and to refrain from engaging in the SSE program or any other new form of exercise. Individuals who were living in care facilities, who were regularly exercising twice or more weekly, had a history of illness or a condition that would affect balance (e.g., stroke or Parkinson's disease), or were unable to participate safely in the exercise program, were excluded.

The Juroku Bank and the University of Nagoya cooperated in the Revitalization of Physical and Social Activities of the Elderly Project and approved the study. All participants gave their informed consent before participating.

#### Outcome measures

Outcome measures were changes in functional fitness related to the risks associated with falling. Fallers are more likely to report difficulty rising from a bed or chair, and to have some form of gait abnormality (11). Lower limb weakness and poor tandem-walking ability have emerged as significant predictive factors among multiple clinical and functional falling risk factors (12). Gehlsen et al. (13) reported that functional fitness in those with a history of falls was lower than in those with no history of falls. In that study, functional fitness items included static balance (one-leg balance test), dynamic balance (backwardwalking test), hip, knee and ankle joint strength, and hip and ankle flexibility tests.

From these studies, we assumed that agility, leg power, locomotion speed, flexibility and balance would be elements of functional fitness related to the risk of falls. Further, in the present study, five functional fitness tests were selected to match each element: standing up from a lying position (agility), chair-stand in 10 seconds (leg power), walking round two cones (locomotion speed), sitand-reach (flexibility), and single-leg balance with eyes closed (balance). Details of the measurements of these fitness items have been reported elsewhere (14, 15). In standing up from a lying position on a signal, participants were asked to stand up as quickly as they could, to a stable erect position from a lying position. The process of moving to the standing position depended on each participant's customary method. Performance time was assessed in terms of time needed to reach a stable erect position. In the item of chair-stand in ten seconds, participants were asked to repeat the exercise of fully standing up and then fully sitting on a chair as many times as possible within ten seconds. During the measurement, participants crossed their arms at the wrists and held them to their chests. Walking round two cones was measured as follows: two cones were placed 1.8 m on both sides of and 1.5 m behind the chair. Participants rose from the chair, walked to the right going inside and round the back of the cone, returned to a fully seated position on the chair, stood up and walked round the left cone, and returned to a fully seated position. One trial consisted of two complete circuits (total distance about 16.8 m). Performance time was recorded in units of 0.1 seconds. In the test of sit-and-reach, participants were asked to sit on the floor and push the plastic cursor forward slowly as far as possible with their middle fingers and without bending their knees. Performance was recorded as the maximum distance between toes and middle fingers; the farther forward the fingers, the greater the performance distance. The reference position, 0 cm, was at the level of the toes. Participants performed twice and the better (further) score indicated by the cursor was noted.

Descriptive variables, such as age, height, weight and attendance rate in the exercise program, were recorded.