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高齢者の転倒予防

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Key words：要介護，転倒スコア，太極拳，個別アセスメント

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高齢者の転倒と寝たきり

高齢者は屋内外，様々な場所で転倒する危険があり，地域での転倒率は20～40％と言われている．また，転倒に伴って大腿骨頸部をはじめとして骨折が生じ，これがもとで寝たきりに陥るケースが多い（図1）．統計的にも，転倒による骨折発生頻度や転倒・骨折によって要介護に至る頻度は，高齢になるほど増加することが判明している[1]．一方，転倒によって骨折やその他の重度な外傷は免れても，再度転倒するのではないかとの不安から，意欲低下や閉じこもり状態になり，やがてADLが低下し，要介護，寝たきり状態に陥る慢性的な経過をたどるケースも多い（図1）．

転倒しやすい高齢者のスクリーニング

転倒には様々な要因がかかわるが，大きく外的要因と内的要因に分けることができる．外的要因とは屋内の段差や障害物，手すりの有無，履き物など環境要因に起因する場合を指す．一方，内的要因とは1）視力，聴力障害，姿勢変化，筋力低下など加齢に伴う虚弱性変化と，2）循環器要因（起立性低血圧など），神経系要因（パーキンソン病，認知症など），筋・骨格系要因（骨粗鬆症，変形性関節症など）などの身体要因，3）薬物によるものなどを指す．転倒にかかわる要因は多岐に渡るため，一つ一つのコンポーネントを分けて評価することは難しい．外来では，問診，診察に加えて，握力や下肢の筋力検査，片足立ち持続時間，継ぎ足歩行，Up and Goテスト，重心動揺検査などを行い，筋力，バランス能，その他を総合的に評価する．しかしながら，これらの検査は機器や時間を要する難点がある．

したがって，一般高齢者の中で転倒のハイリスク者をさがすためには，より簡易な方法を用いることが望ましい．そのために考案されたのが「転倒スコア」である．転倒スコアは自己記入式調査票であり，身体機能に関連する8項目，認知，感覚器，骨運動器に関する7項目，薬の服用1項目，環境要因に関する5項目の計21項目と，過去1年間での転倒歴を問う全22項目から成っている（図2）．大河内らは転倒スコアを用いて，地域高齢者の転倒を前向きに調査し，過去の転倒と4つの質問項目を用いることによって，感度68％，特異度70％で将来の転倒を予測できることを報告している[4]．我々は，杏林大学病院もの忘れセンターの通院患者において，転倒スコアは，片足立ち持続時間，Up and Goテスト，手伸ばし試験，握力，継ぎ足歩行の各検査と有意な相関を示し，しかも将来の転倒を予測する上で，これらの検査を代用できる可能性があることを報告した[5]．転倒ハイリスク者を見出すマススクリーニングツールとして転倒スコアは有用であると期待できる．

転倒予防のストラテジー

高齢者の要介護，寝たきりを防ぐために転倒予防が重要であることは論を待たないが，予防法が十分あるわけではない．先に記したように，転倒には様々な要因がかかわり，しかもこれらは複合して転倒発生にかかわるため，単一の要因に対する介入だけでは一般に不十分である．病院に通っていない「元気な高齢者」に対する将来の虚弱予防と，施設入所中の「虚弱高齢者」とでは，当然転倒予防対策は異なるべきである．虚弱予防として有効な運動に関して，前者に対しては筋力強化訓練など比較的強度の高い運動が有効であり，後者に対しては“転倒しないよう注意しながら”バランス運動などを行うことが効果的である．太極拳はストレッチ，バランス，筋力強化の意味では最も転倒予防にむいており，半数近くまで転倒を減らすことが報告されている（表1）．その

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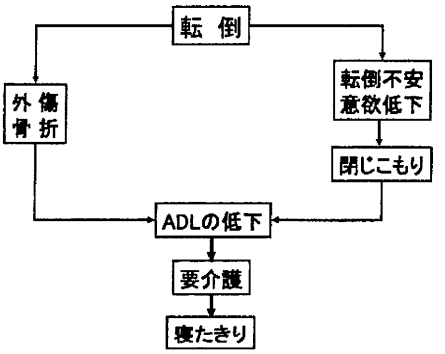

図1　転倒のもたらす影響
鈴木隆雄　老年医学 Update（文献2）より改変

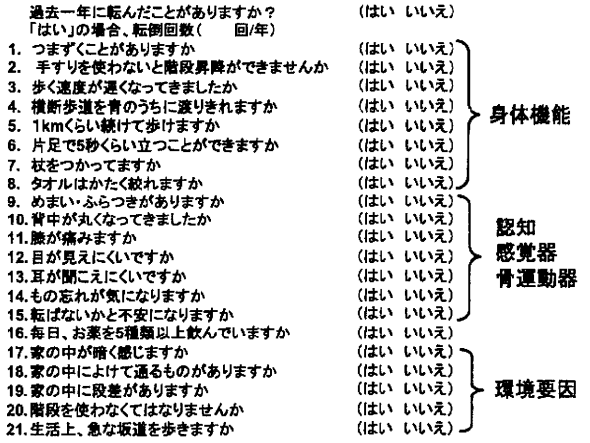

図2　転倒スコア
文献3より

ほか，屋内環境の改善，向精神病薬等の中止，総合機能評価を用いた個別指導なども転倒予防に効果を発揮している（表1）．

医師は，転倒を誘発する可能性のある不必要と思われる薬剤を中止することが重要である．一般に，高齢者は罹患疾患数の増加とともに老年症候群の数が増加し，老年症候群の増加は処方薬剤数の増加につながる．"非特異的と思われる訴え"に対して，薬が手っ取り早く使用されがちだからである．特に，睡眠薬や安定剤，抗うつ薬，抗精神病薬などの薬剤はふらつき，転倒を誘発する薬剤である．また，錐体外路症状を起こすことが知られているメトクロプラミド（プリンペラン），ドンペリドン（ナウゼリン），シサプリド（リサモールなど），スルピリド（ドグマチールなど）などの胃薬は，長期間投与されやすいので，注意が必要である．その他，利尿薬等の各種降圧薬にも転倒誘発の危険がある．いずれの薬剤も，ふらつきのある高齢者を見たら，因果関係を疑って，一つずつ減量，中止していくよう検討する．

表1　転倒骨折予防事業の科学的成績（EBM）

予防事業の種類	研究数	対象数	危険度
家屋環境改善	1	530	0.64
筋力訓練・バランス訓練	3	566	0.80
太極拳	1	200	0.51
向精神薬中止	1	93	0.34
総合機能評価・個別指導	3	1,973	0.73
ヒッププロテクター	6	3,412	0.35

施設高齢者では朝方や，夕食前後の時間帯に転倒が発生することが多い．これは排泄や更衣，整容，食事などに際して移動が多いこと，薄暗い時間であること，注意力が散漫になりやすいこと，などが個人的要因であり，また，介護，看護職員数が少なくなることも大きな原因である．このようなアセスメントに対して，シフト制を導入し，転倒が起こりやすい時間帯に人員を増やすこと，また個別ケアプランを導入することで転倒を減らすことができることが発表されている．

ただ，いかなる手段を講じても，転倒を繰り返す高齢者は存在する．この様な場合，家族に転倒が起こる危険性を十分説明し，骨折→寝たきりの可能性があることを普段からしっかり説明しておく必要がある．そのうえで，転倒しても骨折しないようヒッププロテクター等の装具を着用してもらう．しかしながら，ヒッププロテクターは着心地の悪さのため着用率が上がらないの難点がある．

最後に

転倒は様々な要因が複雑に関連しておこるため，特定の要因を明らかにし，介入することは難しい．個別に，関連要因を抽出し，その中から介入可能な要因，特に環境改善や薬物の整理に十分注意をはらうことができれば，転倒防止への効果は大きい．その際，身近にいる配偶者，家族に注意点を具体的に指示すること，それでも転倒は起こり得ることを説明しておく必要がある．転倒予防に効果がある体操もやり方を間違えれば，転倒を誘発したり，体を痛めてADLを損なう危険もあるので，常に個人に合わせて最善の方法を選択するよう配慮すべきである．

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Fall prevention in the elderly

Koichi Kozaki

Abstract

Causes of falling are multi-factorial. Although it is not easy to identify specific causes of falling, it is necessary to detect the significant causes of falling in each individual. In particular, use of medications and indoor hazards are important factors. We need to give instructions to families who live together with older persons how to avoid dangers of falling. Exercise has been proven to provide beneficial effects to prevent falling, however it is necessary to consider exactly what and how much exercise one should prescribe to elderly individual who are at high risk of falling. In other words, it is important to give best approach to prevent falling after considering the status of the elderly.

Key words: *Dependent elderly, Fall-predicting score, Tai-Chi exercise, Individual assessment*
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MEETING ABSTRACT Open Access

Health measurement for care management using the international classification of functioning codes

J Okochi[1,2*], K Takamuku[1], T Takahashi[3]

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Munich, Germany. 15-18 September 2010

Introduction

Case-mix systems for rehabilitation and geriatric care require information about a patient's functioning. In PCSI 2009, the author presented newly constructed health-measurement scales for elderly persons using the ICF codes. This year, the author presents a method for case-management using ICF-based health-measurement scales in geriatric rehabilitation facilities.

Methods

To construct a care-management tool based on the ICF, we developed 12 ICF-based health-measurement scales including basic behavior, mobility, orientation, communication, cognitive activities, eating function, eating behavior, toileting, bathing, oral hygiene, self-care and clothing.

The new scales have the following characteristics:

1. ICF codes are selected using the Rasch method. Therefore, the items included in the assessment scales are unidimensional and independent of measurement settings.

2. By hierarchically rearranging the items in the assessment scales, the authors constructed Guttman scales. Each Guttman scale is composed of four ICF items, dividing their functioning into five categories. This means that each scale includes only four ICF items, making the measurement simpler and less time consuming.

3. By adding illustrations, the user can identify the functional status of patients.

Results

The case-management tools are as follows:

1. Patients are assigned to one category in each scale.

2. In each scale, the case manager decides whether the patient is more likely to experience an improvement or a worsening of their functional level.

3. If the patient is more likely to improve, an intervention plan, such as rehabilitation or medical intervention, is decided upon. In the case of a patient's worsening, a risk management plan is selected.

Conclusions

When we use conventional ADL assessments, such as FIM or the Barthel index, users can only determine whether they require help for a certain level, such as bed transfer or toileting. With these new tools, we can now have a clear image of whether patients require rehabilitation intervention for improvement, or risk management for preventing a future worsening of their functioning. This was achieved by hierarchically rearranging ICF items and constructing Guttman-type scales according to the item difficulty using the Rasch model.

Therefore, the new ICF-based health-measurements have the following characteristics:

1. A method to simply describe elderly functional level
2. A method to provide standardized care
3. A method to measure change

By using ICF as common taxonomy, these scales are internationally valid and ready to be used as assessment scales worldwide in a geriatric-care setting. In addition, we can now better understand and manage patient care using functional information based on the ICF.

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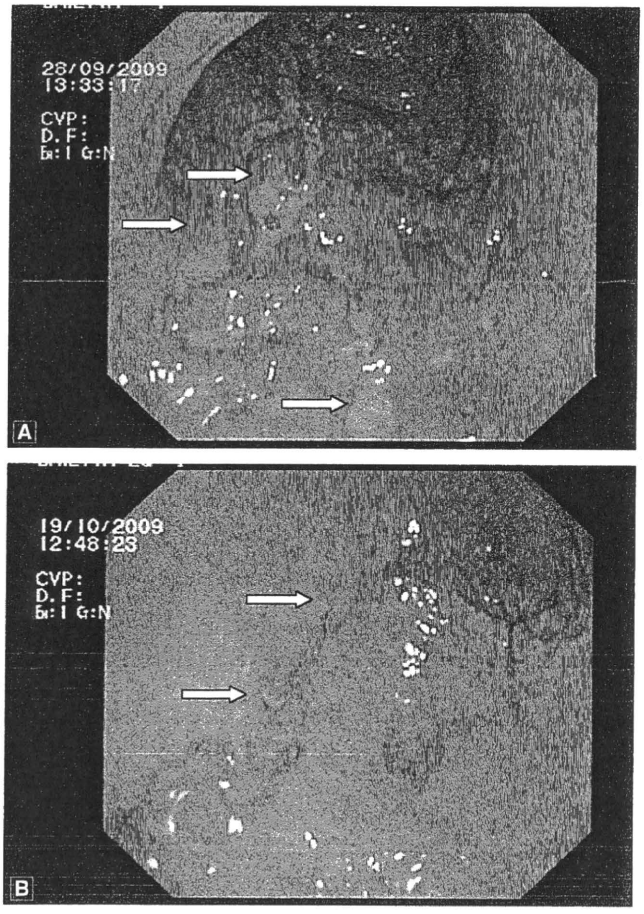

Figure 1. (A) Ulcerations in the left colon (arrows), seen on the first colonoscopy. (B) Colonoscopy after antiviral treatment, ulcerations are in phase of remission (arrows).

DISCUSSION

CMV colitis is a rare cause of diarrhea in older adults; it is more commonly seen in people who are immunosuppressed (with the human immunodeficiency virus or after bone marrow transplant), in whom it is often due to a virus reactivation, or in patients with preexisting inflammatory bowel disease.[4] Nevertheless, although it may be considered an invasive diagnostic test in a frail elderly patient, a sigmoidoscopy with biopsy should be considered as a necessary investigation if culture-negative diarrhea persists. Although some cases of CMV colitis are described in immunocompetent patients, when a diagnosis of CMV colitis is made, screening to exclude the presence of concomitant immunomodulating conditions or inflammatory bowel disease is necessary. In the clinical history of this patient, different coexisting immune-modulating conditions (diabetes mellitus, previous HCV infection, probable essential thrombocythemia) can be identified.

Most cases of CMV infection described in the literature are limited to the left colon, but the infection could theoretically involve all of the digestive tract. In this case, an ulceration was also found in the bulbar duodenum; because the ulcer was bloody, histology was not done, so it was not possible to confirm whether it was a location of CMV infection. Anyway, in a meta-analysis, in which the authors identified 44 cases of CMV bowel infection in immunocompetent patients, the extent of disease was not an independent predictor of survival.[3]

No conclusive statement regarding the need for specific antiviral treatment can be made from the available data in the literature. Although patients with no associated comorbidities seem to have a good rate of spontaneous remission, a trend for higher mortality has been reported in patients aged 55 and older and in patients with diseases affecting immune responses,[3] with a mortality rate of 31.8% in patients aged 55 and older. The patient in the current case belongs to this latter group at high risk of mortality, so it was thought that the antiviral treatment was mandatory. Nevertheless, randomized controlled trials are needed for a more-conclusive answer about antiviral treatment in immunocompetent patients suffering from severe CMV infection.

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EFFECTS OF TESTOSTERONE IN OLDER MEN WITH MILD-TO-MODERATE COGNITIVE IMPAIRMENT

To the Editor: Some population-based studies have found that endogenous testosterone levels are associated with general cognitive function,[1,2] and it has also been reported that testosterone levels are associated with physical and psychological functions, including cognition, in disabled older men,[3] but there have been few studies evaluating the effects of testosterone supplementation in men with cognitive impairment, and the results were inconsistent.[4–7] Thus, additional information is needed for frail or disabled older men with cognitive impairment as the targets of testosterone supplementation. Here, a pilot study to investigate the effect of oral testosterone supplementation for 6 months on

Table 1. Changes in Functional Parameters According to Treatment Group

Functional Parameters	Mean ± Standard Deviation							P-Value
	Testosterone				Control			
	Baseline	3 Months	6 Months	Difference: 0 to 6 Months	Baseline	3 Months	6 Months	Difference: 0 to 6 Months	
Mini-Mental State Examination	20.2 ± 4.5	21.8 ± 4.7	22.6 ± 6.5*	2.4 ± 3.1	21.9 ± 5.3	22.0 ± 4.6	22.0 ± 4.1	0.1 ± 2.7	.03
Hasegawa Dementia Scale, Revised	17.6 ± 5.9	18.2 ± 7.1	20.6 ± 7.3*	3.0 ± 4.3	19.6 ± 5.6	20.1 ± 7.0	18.8 ± 7.7	−0.8 ± 2.3	.02
Barthel Index	91 ± 12	89 ± 17	91 ± 15	0.5 ± 7.1	92 ± 10	91 ± 10	92 ± 7	0.4 ± 7.6	.70
Vitality Index	9.0 ± 0.9	9.3 ± 0.9	7.9 ± 1.3	−1.1 ± 1.0	9.0 ± 1.0	9.4 ± 1.0	9.4 ± 0.9	0.4 ± 1.0	.35

P-values are based on repeated-measures analysis of variance comparing the 6-month change between the groups.
*$P < .05$ compared with baseline.

cognitive function in Japanese older men with mild to moderate cognitive decline is reported.

Eleven men with cognitive impairment, mean age 81 ± 6, receiving long-term care, were assigned to take oral testosterone undecanoate 40 mg daily for 6 months after a breakfast containing 15 to 20 g of fat. The control group of 13 men matched for age and cognitive function were followed without testosterone treatment. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE) and Hasegawa Dementia Scale, Revised (HDS-R) at baseline and at 3 and 6 months. Plasma hormone levels were also measured. The institutional review board approved the study protocol, and all participants or their families gave written informed consent.

At baseline, mean total and free testosterone levels, calculated using the Vermeulen equation,[8] were 14 ± 4 nmol/L and 246 ± 47 pmol/L, respectively. There were no significant differences between the groups in age, length of education, nutritional parameters, functional parameters, or plasma hormone levels. Fasting plasma testosterone levels in the morning did not change significantly during the study, whereas the post-dose levels increased up to 30 ± 8 nmol/L 6 hours after testosterone administration, as reported previously.[9] The changes in functional parameters in each group from baseline to 6 months are shown in Table 1. At 3 months, subjects who received testosterone treatment showed a nonsignificant increase in MMSE and HDS-R scores, whereas at 6 months, cognitive scores were significantly greater than at baseline. In the control group, both cognitive scores remained unchanged. The difference between the groups was significant at 6 months. Prostate-specific antigen and liver function were unchanged, and no adverse effects were observed.

No significant changes were observed in basic activities of daily living (ADL) and ADL-related vitality in either group (Table 1), possibly because these scores were preserved in most subjects at baseline; the Barthel Index and Vitality Index[10] were 91 ± 10 (full score = 100) and 9.0 ± 1.0 (full score = 10), respectively.

This preliminary study needs to be confirmed in a randomized controlled trial with a large sample size. Nevertheless, these results indicate the effects of testosterone treatment on cognitive function in frail elderly men.

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A CASE OF SELECTIVE SEROTONIN REUPTAKE INHIBITOR-INDUCED RAPID EYE MOVEMENT BEHAVIOR DISORDER

To the Editor: Rapid eye movement (REM) sleep behavior disorder (RBD) is often seen in older patients and is characterized by a loss of normal skeletal muscle atonia during REM sleep.[1,2] As a result, the disease manifests as nocturnal motor activity consistent with the enactment of dream content, for example grabbing the bed partner in response to a dream about falling from a cliff. RBD often results in injury to the patient, bed partner, or both.[1,2]

In perhaps up to two-thirds of cases, RBD is associated with neurodegenerative disorders, most notably the alpha-synucleinopathies (Parkinson's disease, Lewy body disease, multiple systems atrophy), often antedating other manifestations of these disorders by many years.[1–4] Other cases seem to be idiopathic, although it has been suggested that various medications, notably selective serotonin reuptake inhibitors (SSRI) and other antidepressants, may commonly induce RBD.[1,4,5] In spite of this assertion, there have been few supporting case reports.[5,6] The authors recently cared for a man who clearly developed RBD as a result of SSRI treatment; the use of the SSRI for posttraumatic stress disorder (PTSD) complicated the clinical picture.

CASE REPORT

An 87-year-old male World War II veteran had been treated for PTSD with associated nightmares but no nocturnal motor activity with bupropion and lorazepam. Past medical history was significant only for essential hypertension. In 1998, after many years of treatment, sertraline was added because of increasing symptoms. Within 6 months of adding sertraline, the patient developed frequent nocturnal motor behavior consistent with the content of his dreams and nightmares, for example punching and choking his wife in the context of a dream about being in a fight. As a result, he and his wife had suffered lacerations and contusions. Other behaviors included running out of his bedroom or running into a window. Upon awakening, he was able to recall portions of the dreams but was unaware of the motor behaviors.

Trials of temazepam, zolpidem, and trazodone were ineffective in improving these behaviors. Ultimately, a diagnosis of RBD was made based on the clinical presentation. Clonazepam 1 mg at bedtime was added, which resulted in a moderate decrease in the frequency of the nocturnal motor activity, from nightly to two or three times per week. After 3 months, sertraline was slowly tapered and discontinued, which resulted in a complete cessation of all nocturnal motor behavior. He remained free of nocturnal motor activity for 5 months, until sertraline was inadvertently restarted after the loss of his wife. Within 1 month of restarting sertraline, the nocturnal motor behavior returned. There has thus far been no evidence of dementia or of parkinsonism.

This patient's clinical presentation was typical of RBD; unfortunately, his and his wife's injuries were also typical. It seems clear that his RBD was SSRI induced; it developed after sertraline was started, did not definitively improve until it was stopped, and recurred after it was inadvertently restarted, and there was no evidence of parkinsonism or dementia over the previous 12 years. Although there are few published cases of SSRI-induced overt RBD, increased electromyography activity during REM sleep has been demonstrated in patients taking SSRIs. (None of the patients were being treated for PTSD.)[7]

The relationship between RBD and PTSD is complex and not fully investigated. There is clinical and polysomnographic evidence of greater motor activity during REM sleep in patients with PTSD,[8] and greater prevalence of RBD was noted in a cohort of patients with PTSD.[9] SSRIs are effective for PTSD-related nightmares[10] but may cause RBD, clonazepam is effective for RBD[1,2,4] but not for PTSD-related nightmares,[10] and RBD is not associated with the typical diurnal symptoms of PTSD. In spite of his long history of PTSD and related nightmares, this patient had never exhibited any significant motor activity during sleep until the SSRI was started.

RBD is relatively common in geriatric practice and should be explored in any patient with nocturnal injuries or motor activity. RBD responds well to treatment, generally with clonazepam. Discontinuation of SSRIs or changing to

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Effects of dehydroepiandrosterone supplementation on cognitive function and activities of daily living in older women with mild to moderate cognitive impairment

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Aim: There is little evidence that dehydroepiandrosterone (DHEA) has beneficial effects on physical and psychological functions in older women. We investigated the effect of DHEA supplementation on cognitive function and ADL in older women with cognitive impairment.

Methods: A total of 27 women aged 65–90 years (mean ± standard deviation, 83 ± 6) with mild to moderate cognitive impairment (Mini-Mental State Examination, MMSE; 10–28/30 points), receiving long-term care at a facility in Japan were enrolled. Twelve women were assigned to receive DHEA 25 mg/day p.o. for 6 months. The control group ($n = 15$) matched for age and cognitive function was followed without hormone replacement. Cognitive function was assessed by MMSE and Hasegawa Dementia Scale-Revised (HDS-R), and basic activities of daily living (ADL) by Barthel Index at baseline, 3 and 6 months. Plasma hormone levels including testosterone, DHEA, DHEA-sulfate and estradiol were also followed up.

Results: After 6 months, DHEA treatment significantly increased plasma testosterone, DHEA and DHEA-sulfate levels by 2–3-fold but not estradiol level compared to baseline. DHEA administration increased cognitive scores and maintained basic ADL score, while cognition and basic ADL deteriorated in the control group (6-month change in DHEA group vs control group; MMSE, +0.6 ± 3.2 vs −2.1 ± 2.2, $P < 0.05$; HDS-R, +2.8 ± 2.8 vs −0.3 ± 4.1, $P < 0.05$; Barthel Index, +3.7 ± 7.1 vs −2.7 ± 4.6, $P = 0.05$). Among the cognitive domains, DHEA treatment improved verbal fluency ($P < 0.05$).

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Conclusion: DHEA supplementation in older women with cognitive impairment may have beneficial effects on cognitive function and ADL. **Geriatr Gerontol Int 2010; 10: 280–287.**

Keywords: activities of daily living, cognitive function, dehydroepiandrosterone.

Introduction

Dehydroepiandrosterone (DHEA) and its sulfate (DHEA-S) are the most abundant circulating steroids mainly produced by the adrenal zona reticularis in both sexes.[1] Their circulating levels decline with advancing age,[1–4] and there has been growing public interest in DHEA supplementation to prevent age-associated physical and cognitive impairment. DHEA is considered a crucial precursor of human sex steroid biosynthesis, and to exert indirect androgenic and estrogenic effects following conversion into smaller amounts of testosterone and estradiol.[5,6] While this conversion contributes to a part of testosterone production in men, its role may be much more significant in postmenopausal women whose ovarian production of androgen and estrogen has waned. Importantly, postmenopausal women with intact ovaries continue to produce androgens; DHEA(-S), testosterone and androstenedione, while their production of estradiol is minimal.[7] However, the role of androgens in older women's health is not fully understood.

Clinical trials of the effects of estrogen replacement therapy on cognitive function have shown a lack of efficacy in postmenopausal women initiating hormone replacement therapy after the age of 65 years.[8,9] On the other hand, previous reports have suggested that DHEA may have neuroprotective effects, and the age-associated DHEA(-S) decline is associated with cognitive impairment in older women.[2,10–12] One longitudinal study observed lower DHEA-S levels in patients who subsequently developed Alzheimer's disease.[13] However, controlled trials with DHEA supplementation have failed to show beneficial effects on cognition in healthy middle-aged to older women.[14–16] In these studies, the participants were limited to those who did not have cognitive impairment; therefore, it is reasonable to hypothesize that DHEA supplementation may be effective in much older women with cognitive decline as well as lower DHEA levels.

Dehydroepiandrosterone deficiency is also considered to be involved in the development of physical frailty.[17] Clinical experience with DHEA supplementation in older women is limited, and the few clinical trials examining its effect on physical function and activity of daily living (ADL) have yielded inconsistent results.[18–20] Evidence is lacking for much older women in whom physical impairment becomes more apparent and is accompanied by an age-associated DHEA decline. In our previous study, plasma DHEA and DHEA-S levels, but not estradiol level, were independently related to higher basic ADL in older women aged 70–93 years with functional decline receiving long-term care.[21] We hypothesized that in older women, DHEA replacement could be effective for the age-related decline of physical as well as psychological function.

This study therefore examined the effect of relatively low-dose (25 mg daily) p.o. DHEA supplementation for 6 months on cognitive function and ADL in older women with cognitive impairment.

Methods

Subjects and study design

In this open, non-randomized controlled study, 27 women aged 65 years or older who attended a health service facility for the elderly (a facility that provides nursing care and rehabilitation services to elderly people with disability, Mahoroba-no-Sato, located in Nagano Prefecture, Japan) were enrolled. The participants were in a chronic stable condition and receiving Long-term Care Insurance service either for admission to the facility or day-care services. The principal inclusion criteria were mild to moderate cognitive decline; both Mini-Mental State Examination (MMSE)[22] and Hasegawa Dementia Scale-Revised (HDS-R)[23] scores were between 10 and 28. The subjects were diagnosed as having a mild cognitive impairment[24] or Alzheimer's disease according to the Diagnostic and Statistical Manual of Mental Disorders IV.[25] The participants had never been treated with hormone replacement therapy, and plasma DHEA-S concentration was less than 3.0 μmol/L. The exclusion criteria were history of stroke, extremely low ADL status (Barthel Index[26] <50), malnutrition (serum albumin <3.5 mg/dL), malignancy, acute inflammation (fever, white blood cell count >10 000/μL, or other signs of infection within 4 weeks before enrollment) and overt endocrine diseases, because these diseases may affect both plasma sex hormone levels and functions. None of the subjects were taking a cholinesterase inhibitor (donepezil hydrochloride) or glucocorticoid, opiate or hormone supplement.

Twelve women were assigned to receive DHEA capsule (25 mg/day, Athena Clinics International,

Honolulu, HI, USA) and 15 women were followed up without any additive medication. Medications that could influence cognitive function and plasma hormone levels were not changed during the study period. Outcome measures were cognitive function, ADL, plasma hormone levels, blood cell counts, blood chemical parameters and subjective adverse events. They were assessed at baseline, and after 3 and 6 months. The institutional review board of Mahoroba-no-Sato approved the study protocol, and all participants or their families gave written informed consent.

Hormone measurements

Blood samples were obtained from the participants in the morning after an overnight fast, and plasma hormone levels in addition to blood cell counts and blood chemical parameters were determined by a commercial laboratory (Health Sciences Research Institute, Yokohama, Japan). DHEA and DHEA-S were assayed using sensitive radioimmunoassays with minimum detection limits of 0.04 ng/mL (0.14 nmol/L) and 2.0 μg/dL (0.05 μmol/L), respectively. Total testosterone and estradiol were assayed using chemiluminescent immunoassays with minimum detection limits of 7 ng/dL (0.2 nmol/L) and 4 pg/mL (14.7 pmol/L), respectively. The intra-assay coefficients of variation for these measurements were less than 5%.

Cognitive function

Trained examiners administered two standardized cognitive function tests, MMSE[22] and HDS-R,[23] to assess multiple, diverse aspects of cognitive function at baseline and at the 3- and 6-month visits. Both scores range 0–30, with higher scores indicating better performance. HDS-R includes questions about the subject's age, orientation, immediate recall, serial subtraction of 7 s, reciting digits backward, recalling three words, recalling five objects and word fluency (generating names of vegetables). MMSE evaluates five aspects of cognition: (i) orientation; (ii) registration; (iii) attention and calculation; (iv) recall; and (v) comprehension of spoken language (naming objects, spoken language ability, following commands). MMSE, but not HDS-R, includes four performance tests: (i) three-stage command; (ii) reading and following a command; (iii) writing; and (iv) construction drawing). Based on the results of HDS-R and MMSE, we evaluated seven cognitive domains (points) as follows: (i) orientation (10); (ii) verbal memory (9); (iii) attention and calculation (5); (iv) visual memory (5); (v) spoken-language comprehension (9); (vi) verbal fluency (5); and (vii) performance (7).

Other functional parameters and anthropometric measures

Trained nurses and physical therapists visited the participants at the facility and performed the assessments. Basic ADL was assessed by Barthel Index,[26] mood by Geriatric Depression Scale (GDS, 15 items),[27] and ADL-related vitality by Vitality Index (10-point scale).[28] Higher GDS scores indicate a more marked self-reported depressive status, while higher Vitality Index scores indicate greater willingness.

Adverse events

Information regarding adverse events was obtained by questioning or examining the subjects. At each visit during the treatment period, all new complaints and symptoms were recorded. The safety of DHEA supplementation was assessed from the symptoms and by measuring blood chemical parameters including liver and kidney function, electrolyte levels and hematological parameters. Preexisting complaints or symptoms that increased in intensity or frequency during the treatment period also were examined.

Statistical analysis

Data were analyzed using SPSS statistical software ver. 17.0. Changes in outcome measures at 3 and 6 months were calculated by comparing the values at baseline with those at each measurement. Within each group, the significance of the change from baseline to 6 months was tested using paired Student's *t*-test. Repeated-measures ANOVA was used to test the statistical significance of the effects of DHEA versus control. Significance tests were two-sided, with an α-level of 0.05.

Results

Hormone changes and adverse effects

Characteristics and hormone levels at baseline according to treatment groups are shown in Table 1. There were no significant differences between the DHEA group and the control group in age, length of education, nutritional parameters, functional parameters and plasma hormone levels. DHEA supplementation was well tolerated, with high adherence, and there were no detectable adverse events and none of the subjects dropped out during the study. Measures of liver function, kidney function, electrolyte levels and hemoglobin level were not significantly altered by treatment with DHEA (data not shown). Body mass index remained unchanged in both groups.

Subjects in the DHEA group showed a significant increase from baseline to 3 and 6 months in levels of

Table 1 Participant characteristics at baseline

	DHEA	Control
No. of subjects	12	15
Age, years	82 ± 6 (69–90)	83 ± 6 (65–89)
Education, years	8 ± 2	8 ± 2
Nutritional parameters		
Body mass index, kg/m^2	22.0 ± 2.4 (18.8–26.4)	22.4 ± 3.2 (17.6–27.1)
Albumin, g/dL	4.4 ± 0.3 (3.7–4.9)	4.3 ± 3.2 (3.8–4.7)
Total cholesterol, mg/dL	227 ± 39 (166–294)	203 ± 22 (173–250)
Functional parameters		
MMSE	24.0 ± 4.2 (18–28)	23.4 ± 4.4 (14–28)
HDS-R	19.9 ± 5.8 (10–28)	21.7 ± 5.6 (10–28)
Barthel Index	89.6 ± 9.4 (55–100)	89.7 ± 6.4 (75–100)
Vitality Index	9.8 ± 0.6 (8–10)	9.9 ± 0.3 (9–10)
GDS	7.0 ± 4.4 (1–15)	7.0 ± 4.0 (1–13)
Hormones		
DHEA-S, μmol/L	1.8 ± 0.6 (0.7–2.4)	1.6 ± 0.8 (0.3–2.9)
DHEA, nmol/L	7.6 ± 4.7 (2.4–19.1)	6.6 ± 3.1 (2.1–11.5)
Testosterone, nmol/L	1.4 ± 0.4 (0.9–2.3)	1.3 ± 0.9 (0.2–3.8)
Estradiol, pmol/L	88 ± 52 (15–187)	70 ± 26 (45–115)

Values are shown as mean ± standard deviation (range). HDS-R, Hasegawa Dementia Scale-Revised; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; DHEA-S, dehydroepiandrosterone sulfate; DHEA, dehydroepiandrosterone. There was no significant difference in each parameter between the groups.

circulating DHEA, DHEA-S and testosterone, with levels reaching approximately 2–3-fold higher than those at baseline, whereas the increase in estradiol level was not significant (Table 2). Subjects in the control group showed no significant change in hormone levels.

Changes in cognitive function and ADL

The changes in functional parameters in each group from baseline to 6 months are shown in Table 2. After 6 months, mean HDS-R score significantly improved in the DHEA group while it remained unchanged in the control group. Mean MMSE score significantly declined in the control group while it remained unchanged in the DHEA group. As a result, significant differences were found in these scores between the groups. DHEA treatment maintained Barthel Index score, whereas the score deteriorated significantly during 6 months in the control group, although the between-group difference at 6 months was not statistically significant. Regarding the components of Barthel Index, in the control group, the sum score of mobility deteriorated significantly after 6 months compared to baseline, while no significant change was observed in the sum score of self care (Table 3). Neither Vitality Index nor GDS changed significantly in both groups.

Table 4 shows the cognitive domain scores at baseline and at 3- and 6-month follow up. Among the seven cognitive domains, DHEA treatment improved verbal fluency ($P < 0.05$), resulting in a significant difference at 6 months between the groups. Verbal memory showed a non-significant trend towards improvement in the DHEA group. Performance test scores significantly declined over time in both groups. There were no differences between the groups in the scores of orientation, attention and calculation, visual memory and spoken-language comprehension.

Discussion

Daily administration of DHEA 25 mg for 6 months in elderly women with mild to moderate cognitive impairment improved cognitive function and maintained basic ADL, compared to the control group. Among the cognitive domains, DHEA significantly improved verbal fluency. At baseline, DHEA and DHEA-S levels were lower than those reported in healthy postmenopausal women in both groups,[2,4] and DHEA treatment increased DHEA, DHEA-S and testosterone levels by 2–3-fold to the mid-normal range for premenopausal

Table 2 Changes in hormone levels and functional parameters by treatment group

	DHEA				Control				*P*
	Baseline	3 months	6 months	0–6-month difference	Baseline	3 months	6 months	0–6-month difference	
Hormones									
DHEA-S, μmol/L	1.8 ± 0.6	4.5 ± 1.3*	5.6 ± 2.9*	3.8 ± 2.8	1.6 ± 0.8	1.8 ± 1.0	1.7 ± 0.8	−0.02 ± 0.4	<0.01
DHEA, nmol/L	7.6 ± 4.7	12.2 ± 4.8*	13.7 ± 7.7*	6.1 ± 8.2	6.6 ± 3.1	7.3 ± 3.7	7.4 ± 4.5	0.9 ± 2.8	0.04
Testosterone, nmol/L	1.4 ± 0.4	2.3 ± 0.7*	2.3 ± 0.8*	0.9 ± 0.8	1.4 ± 0.7	1.4 ± 0.7	1.6 ± 0.8	0.2 ± 0.5	<0.01
Estradiol, pmol/L	88 ± 52	92 ± 48	101 ± 37	13 ± 51	70 ± 26	68 ± 20	67 ± 42	−4.0 ± 38	0.17
Functional parameters									
MMSE	24.0 ± 4.2	24.1 ± 4.6	24.6 ± 4.3	0.6 ± 3.2	23.4 ± 4.4	23.1 ± 5.4	21.3 ± 5.0**	−2.1 ± 2.2	0.04
HDS-R	19.9 ± 5.8	20.5 ± 7.3	22.7 ± 6.3**	2.8 ± 2.8	21.7 ± 5.6	22.1 ± 5.6	21.3 ± 6.4	−0.3 ± 4.1	0.04
Barthel Index	89.6 ± 9.4	92.7 ± 6.5	93.3 ± 6.8	3.7 ± 7.1	89.7 ± 6.4	86.9 ± 7.2	87.0 ± 6.7*	−2.7 ± 4.6	0.04
Vitality Index	9.8 ± 0.6	9.7 ± 0.5	9.7 ± 0.7	−0.1 ± 1.0	9.9 ± 0.3	9.8 ± 0.5	9.7 ± 1.0	−0.3 ± 1.0	0.80
GDS	7.0 ± 4.4	6.2 ± 3.4	6.6 ± 3.7	−0.4 ± 1.7	7.0 ± 4.0	8.3 ± 3.9	7.5 ± 3.5	0.5 ± 3.3	0.60

Values are shown as mean ± standard deviation (range). *P*-values are for repeated-measure ANOVA over all three time points. DHEA, dehydroepiandrosterone; HDS-R, Hasegawa Dementia Scale-Revised; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; DHEA-S, dehydroepiandrosterone sulfate; DHEA, dehydroepiandrosterone. **$P < 0.01$ compared to baseline, *$P < 0.05$ compared to baseline.

women.[2] No detectable adverse effects were observed throughout the study.

According to the previous trials, DHEA supplementation of 50 mg or more daily does not provide beneficial effects on cognition in healthy middle-aged to elderly women without cognitive impairment.[14–16] However, in a small-scale randomized double-blind placebo-controlled study, DHEA transiently improved cognition (after 3 months) in subjects with Alzheimer's disease while the improvement was not significant at 6 months.[29] Preliminary analysis of the small number of subjects in the present study suggested that DHEA treatment was no less effective in subjects with low baseline cognitive function than those with higher cognitive function (data not shown). Whether the effects of DHEA might be influenced by baseline cognitive function should be further investigated.

It is noteworthy that the 6-month effect of donepezil hydrochloride (5 or 10 mg), the only cholinesterase inhibitor used in Japan, in patients with Alzheimer's disease ranged from no change to less than 1 point improvement in MMSE score,[29–33] which is not so different from the effect of DHEA observed in the present study.

In the present study, not only the participants' cognitive function was impaired, but baseline plasma DHEA(-S) level was also low compared to that in postmenopausal or perimenopausal women.[2,4,10] Regarding DHEA-S levels, according to a report in which healthy pre- and postmenopausal women were studied, DHEA-S levels in women aged 35–44 years and 45–55 years were as follows: 4.31 ± 2.11, 3.90 (mean ± standard deviation) and 3.42 ± 2.01 μmol/L.[2] In this study, DHEA-S was measured using chemiluminescent enzyme immunometric assay; although the measurements by this method and those by radioimmunoassay have been reported to be comparable. In our study, DHEA treatment increased DHEA-S levels to the mid-normal range for premenopausal women.[2] Also, the subjects with lower baseline DHEA-S levels showed non-significant trend towards more improvement in cognitive scores (data not shown). Thus, future studies are needed to explore whether the effects of DHEA might be influenced by baseline DHEA levels.

Because the DHEA receptor has not been identified, DHEA may act after conversion to testosterone and subsequently estradiol through estrogen receptors and androgen receptors, both of which are found in the hippocampus and frontal lobes and subserve verbal memory and working memory in women.[34,35] Further, hippocampal volume and perfusion have been shown to correlate with serum DHEA-S level in demented patients.[36,37] It has also been suggested that estrogenic and androgenic derivatives of DHEA might have different effects on cognitive functions.[38] However, the mechanism by which DHEA improves cognitive

Table 3 Changes in mobility and self-care scores in Barthel Index during the study

Domains (points)	Mean ± SD Baseline	3 months	6 months	Change (0–6 months)	*P*
Mobility (55)					
DHEA	46.9 ± 9.2	48.2 ± 6.0	49.2 ± 5.2	2.3 ± 5.4	0.01
Control	47.5 ± 5.4	46.2 ± 5.5	45.0 ± 4.3*	−3.7 ± 3.9	
Self care (45)					
DHEA	42.7 ± 6.1	44.5 ± 1.5	43.1 ± 2.5	0.4 ± 6.9	0.96
Control	41.8 ± 4.2	42.5 ± 3.4	41.2 ± 4.3	0.7 ± 3.2	

Mobility is the sum score of five domains: (i) transfer (moving from a bed to a wheelchair and back); (ii) walking on a level surface; (iii) propelling a wheel chair; (iv) ascending and descending stairs; and (v) bathing and toilet use. Self care includes feeding, grooming, dressing, bowels and bladder. *P*-values are for repeated-measure ANOVA over all three time points. $^{*}P < 0.05$ compared to baseline. SD, standard deviation.

Table 4 Changes in cognitive domain scores during study

Domains (points)	Mean ± SD Baseline	3 months	6 months	Change (0–6 months)	*P*
Orientation (10)					
DHEA	8.3 ± 1.9	8.0 ± 2.7	7.5 ± 3.0	−0.1 ± 1.2	0.28
Control	8.3 ± 1.9	8.0 ± 2.8	7.5 ± 2.9	−0.7 ± 1.7	
Verbal memory (9)					
DHEA	5.7 ± 2.1	6.5 ± 2.3	6.7 ± 2.5†	1.0 ± 1.9	0.79
Control	6.5 ± 1.7	7.5 ± 1.8	7.0 ± 1.9	0.5 ± 1.7	
Attention and calculation (5)					
DHEA	2.3 ± 1.9	2.8 ± 2.0	2.7 ± 1.8	0 ± 2.3	0.79
Control	2.0 ± 1.7	1.9 ± 1.2	1.8 ± 1.5	−0.5 ± 1.4	
Visual memory (5)					
DHEA	3.6 ± 0.9	3.6 ± 1.3	3.8 ± 1.2	0.3 ± 1.1	0.91
Control	3.6 ± 1.3	3.9 ± 0.9	3.9 ± 1.0	0.5 ± 1.1	
Language comprehension (9)					
DHEA	8.5 ± 0.8	7.8 ± 2.5	8.7 ± 0.7	0.1 ± 0.3	0.12
Control	8.5 ± 0.8	8.5 ± 0.8	8.4 ± 1.1	−0.1 ± 0.9	
Verbal fluency (5)					
DHEA	2.8 ± 3.3	2.5 ± 2.0	4.3 ± 1.1*	1.5 ± 1.7	0.01
Control	3.2 ± 1.9	3.8 ± 1.6	3.3 ± 1.9	0.1 ± 2.1	
Performance (7)					
DHEA	5.7 ± 0.7	5.5 ± 0.7	4.8 ± 0.4**	−0.8 ± 0.6	0.36
Control	5.6 ± 0.6	5.1 ± 0.6	4.5 ± 0.9**	−1.1 ± 0.8	

Change refers to score change during 0–6 months for each parameter in each treatment group. *P*-values are for repeated-measure ANOVA over all three time points. DHEA, dehydroepiandrosterone. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{\dagger}P < 0.1$ vs baseline. SD, standard deviation.

function is unknown. In the present study, plasma estradiol level was not significantly increased after DHEA treatment, implying that its beneficial effects on cognition might be androgen-dependent. Unfortunately, free testosterone levels were not measured, because they were considered to be undetectable in many cases in older women. In addition, sex hormone-binding globulin (SHBG) measurement was not available; however, it has been reported that DHEA 50 mg treatment for 3 months in postmenopausal women did not significantly change SHBG levels,[39] suggesting that the change in SHBG-bound hormone levels after DHEA treatment might be minimal. Given the local aromatization of androgen to estradiol in the brain, the effect of DHEA on cognition might be indirect, complex and heterogeneous. The molecular mechanism underlying the association

between DHEA and cognitive function needs to be clarified, and active forms of testosterone and estradiol should also be examined to investigate whether they would change after DHEA administration.

In our previous study, plasma DHEA and DHEA-S levels were independently related to higher basic ADL in older women aged 70–93 years with functional decline,[21] and other reports have shown a correlation between DHEA level and muscle mass, strength and physical performance.[40,41] In the present study, DHEA treatment maintained the Barthel Index score, while the score deteriorated significantly in the control group. Regarding body composition and strength, DHEA administration in postmenopausal older women aged up to 80 years did not alter body composition, physical performance or strength.[18–20] However, in one small-scale open-label trial, DHEA treatment for 4 weeks improved ADL in three out of seven patients (both men and women) with multi-infarct dementia.[42] All these studies are preliminary, and large-scale and long-term studies are required to ascertain whether DHEA could have a beneficial effect on ADL in older women.

In the present study, no effect of DHEA on depressive mood or vitality was observed, consistent with most clinical trials in older women.[15,43,44] This might be attributable to the participants' relatively low depressive status and high vitality status, namely, ceiling effects.

The limitations of our study should be acknowledged. First, this study was neither blinded nor randomized. Second, the number of participants was too small to confirm the results. Thus, results need to be confirmed by large-scale randomized trials to exclude possible selection bias. Third, considering the sensitivity and accuracy, a standard test like the Alzheimer's Disease Assessment Scale should be used in clinical trials to ascertain the effect of DHEA. Finally, our study duration was 6 months so it does not provide any information on the effects of longer-term DHEA supplementation.

In summary, this small study showed that supplementation of DHEA 25 mg for 6 months to older women with mild to moderate cognitive impairment improved cognitive scores and maintained basic ADL. The results should be confirmed in large-scale randomized trials.

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地域在住高齢者におけるサルコペニア改善のための運動，アミノ酸補充の効果

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Effects of exercise and amino acid supplementation for sarcopenia in community-dwelling elderly people

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はじめに

人間の緒機能は，常に変化する属性を持ち，個体の潜在能力が効率よく発揮できる方向へ変えていくのが一般的である。しかし，中年期を過ぎると様々な組織の機能が十分発揮できなくなり，環境変化への適応能力の低下ないしは機能喪失が徐々に増してくる。その背景要因の一つに，体脂肪やLBM（lean body mass）の変化が挙げられる[1)]。中でも，骨格筋量の減少（Sarcopenia）[2)]は，筋力の衰え，身体機能の低下をもたらし，身体的障害あるいは老年症候群の発症と密接に関わっていることが多くの疫学調査で指摘されている。骨格筋量の減少には性，年齢，身長，体重，BMI，テストステロン，脂肪量，不活動，ビタミンD，低栄養など様々な要因が複雑に関わっている[3,4)]。サルコペニア予防策を構築するためには，多くの危険因子の中で，可変因子の改善を目的とした取組みが有効であり，Fiataroneら（1994）は，骨格筋の不使用と低栄養の改善に焦点を当てた介入が有効であると指摘している[5)]。

サルコペニア予防のための戦略

加齢に伴う骨格筋量の減少を予防したり，委縮した骨格筋の機能を回復させるためには，筋に適当な刺激を与えるトレーニングが有効的と考える。しかし，虚弱高齢者を対象とする場合には，筋力発揮に伴うメカニカルストレスの増大や循環器への負担が懸念され，無理のないトレーニングが原則である。運動効果について調べた研究によれば，日常的活動レベルが低く，筋力低下が進んでしまった虚弱高齢者であっても筋力増大の効果が報告されている。虚弱高齢者における著しい筋力増大効果は，筋肥大よりも神経系の機能改善に起因するものと考えられてきた。しかし，最近の研究により高齢者でも筋肥大が起こることが確かめられている[5)]。

Fiataroneら（1994）は，72～98歳の長期施設入所者100名を対象に，筋力強化運動，栄養補充効果を検証した。その結果，筋力強化運動群では筋力113%（P<0.01），歩行速度11.8%（P=0.02），階段昇降機能28.4%（P=0.01）と有意に上昇したが，太腿の筋断面積2.7%（P=0.11）増加に止まった。一方，240mlの栄養補充（炭水化物60%，脂肪23%，タンパク質17%）の効果は検証されなかったと指摘している[6)]。これらの結果は，サルコペニアの改善のためには単なる栄養補充ではなくて，骨格筋量の減少メカニズムを把握した上での処置が必要であることを示唆する試験である。高齢者における骨格筋量の減少（サルコペニア）背景は，高齢者では，筋タンパク質の合成と分解が減弱し，その結果としてサルコペニアが起こるということである。よって，骨格筋量の予防・改善には筋タンパク質合成促進が有効と考える。骨格筋タンパク質合成は血液中のアミノ酸濃度に影響され，血液中のアミノ酸濃度が上昇すると筋タンパク質合成速度が速やかに増加するが，分解速度は変化しないことが指摘されている[7)]。特に，高ロイシン含量の必須アミノ酸は比較的少量で筋タンパク質合成が促進されることを検証したことから，その長期摂取による骨格筋量の改善が期待できる[8)]。

サルコペニア改善のための運動，アミノ酸補充の効果

1）サルコペニア高齢者の特徴

これらの背景を踏まえて，筆者は，サルコペニアと判定された304名と正常者1,095名の調査項目を比較し，サルコペニア高齢者の特徴を調べた。その結果，サルコペニア群は正常群に比べて，年齢が高く，下腿三頭筋周囲，BMI，筋肉量が有意に低値を示すとともに，健康度自己

表１．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

評価，定期的な運動習慣を持っている者の割合は低かったが，外出頻度低下者の割合は高かった。一方，既往歴においては，貧血症，骨粗鬆症，骨折歴は有意に高かったが，高血圧症，高脂血症は正常群より低かった（表１）。

２）運動，アミノ酸補充の効果

サルコペニア改善のための運動，アミノ酸補充の効果を検証するために，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ヶ月間実施した。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１），地域在住サルコペニアの改善には運動のみならずアミノ酸補充も有効であることが示唆された。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

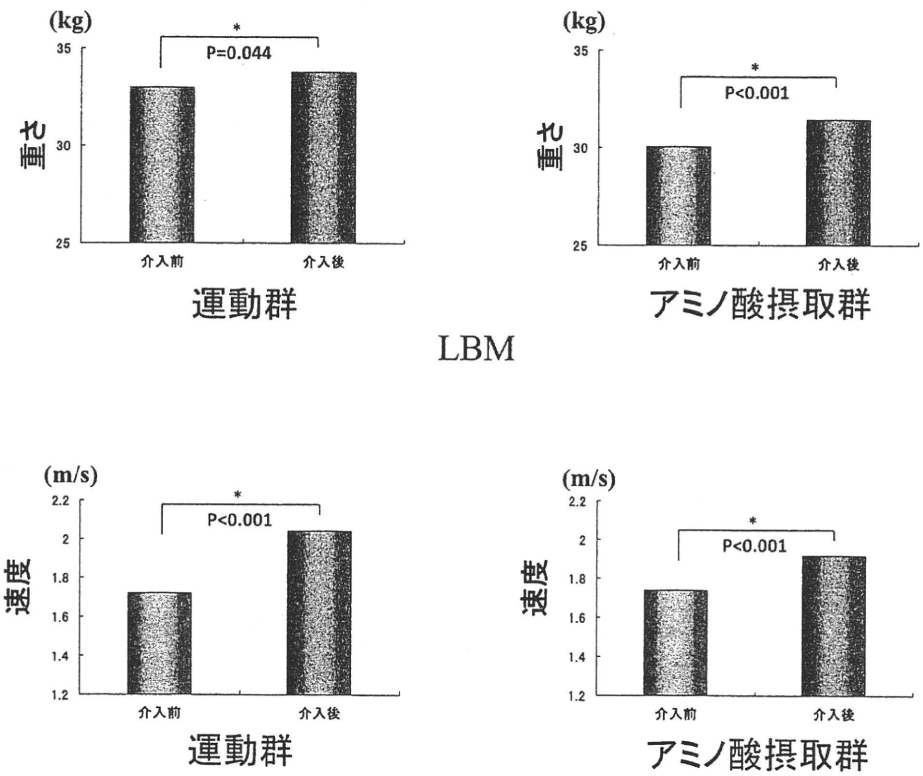

図１．３ヶ月間の運動，アミノ酸摂取の介入がLBMおよび歩行速度に及ぼす影響

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見られなかった。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，運動指導あるいは栄養補充の両方と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のためには，運動介入の効果が優れる可能性が示唆された。

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予防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見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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特集 ロコモティブシンドロームと生活習慣病

3．ロコモティブシンドロームの発症メカニズム
4）サルコペニアとロコモティブシンドローム

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はじめに

人間の諸機能は，中年期を過ぎると低下ないしは喪失が徐々に増してくる．その背景要因の1つに，体組成の変化が挙げられる．加齢に伴う体組成の変化の中で，最も特徴的なのは脂肪組織量の増加と，骨や骨格筋を含んだ徐脂肪組織量(fat-free mass：FFM)の低下である．加齢に伴うFFMの変化は，男性で0.34 kg/yr，女性で0.22 kg/yr減少することが[1]，筋肉量は，男性で0.19 kg/yr，女性で0.11 kg/yr減少するが，50歳代以降では下肢骨格筋量の減少が顕著であることが指摘されている[2]．加齢に伴って筋肉量や骨格筋量が減少すると，筋の質を表す筋力の衰弱をもたらし，特に下肢筋力の衰えは歩行機能を著しく低下させ，ひいては転倒・骨折の原因となるなど，高齢者の移動能力を制限してしまう重大な要因である．

一般的にロコモティブシンドローム(以下，ロコモ)は，運動器の障害のため移動能力の低下を来し要介護状態になっていたり，要介護状態になる危険性の高い状態を指す概念である．身体活動は骨，筋肉，関節，神経などの組織や器官の機能的連合によって産出される結果であり，どれか1つ不具合になっても上手く働かない．

ここでは，ロコモとサルコペニア(sarcopenia)に共通の媒介要因として考えられる筋力の衰えという観点から，ロコモとサルコペニアの関連性や位置づけについて簡単に紹介する．

表1　性・年齢・人種別にみたサルコペニアの有症率

年齢群(歳)	男性 ヒスパニック (n＝221)	男性 白人 (n＝205)	女性 ヒスパニック (n＝209)	女性 白人 (n＝173)
＜70	16.9	13.5	24.1	23.1
70～74	18.3	19.8	35.1	33.3
75～80	36.4	26.7	35.3	35.9
＞80	57.6	52.6	60.0	43.2

(文献4より引用)

サルコペニアの定義および有症率

加齢に伴って徐々に起こり得る筋肉量の減少や筋力の衰えを表す言葉として「sarcopenia」が1989年以降使用され[3]，老年症候群の発症と深く関わっていることから注目されるようになっている．

現在サルコペニアの操作的定義として広く用いられているものの1つとしては，Baumgartnerらの定義がある．この定義は，二重エネルギーX線吸収法(dual energy x-ray absorptiometry, DXA)から求めた四肢の筋量(appendicular skeletal muscle mass：ASM)を身長(m^2)で除したskeletal muscle mass index(SMI)を指標としたものである．サルコペニアの定義は，18～40歳成人のSMI平均より2 SD以下の場合とされている．この定義に基づく有症率は，70歳以下の高齢者で13.5～24.1%の範囲であるが，80歳以上になると43.2～60.0%に上昇する(表1)．さらに，サルコペニアのカットポイントは，SMIが男性で7.26 kh/m^2，5.45 kg/m^2と