- 2) 通常の臨床で行なわれる薬物治療の可能性が少ない。しかし比較的長期間にわたる身体機能のトレーニングにより症候の改善や抑制が可能である。
- 3) 治療効果や評価が困難である。しかし最も重要なことは対象者である高齢者本人が減衰した機能の改善を実感し、ADLの拡大とQOLの向上が実感できることである。

#### III. 高齢社会における新しい取り組みの重要性

上述のように、老年症候群は日々の生活において健康 度を低下させ、自立を阻害し、生活の質(QOL)を著し く損なうことは明らかであり、これらの早急な対策が必 要となる。

我が国のこれまでの健診(検診)は主として中高年齢層に対し、生活習慣病を対象として早期発見、早期治療を目的として行なわれている。このような全国民を対象とする効率的な健診システムを発展させ実施してきたことが、国民の健康の総合的な改善と世界に冠たる長野国を生み出してきたという誇るべき実績がある。このこと自体は高く評価すべきであり、今後とも生活習慣病の制圧に向けて一層受診率を向上させ、疾病把握のために感度と特異度を上げ、精度へ高い検診が行なわれるべきことは明白である。

しかし、高齢期の健康と生活機能の維持、そして生活の質 (QOL) の向上のためには、現在の疾病だけを対象とする検診だけは不十分である。約80歳という平均寿命をこえて生存した高齢者の死亡の大きな要因は必ずしも疾病ではなく、全身的な心身の虚弱にこそ大きな問題が存在するか。そのためにも高齢期には日々の生活での障害要因、すなわち老年症候群を早期に発見し、早期に対処し、総合的な健康を維持するための、新しい健診システムの構築が必須の状況となっている。このような観点から、我々は高齢者の健康長寿を目的とした「お達者健診」を開発し実施しているか。

「お達者健診」では、罹患率の高い慢性疾患についても 当然チェックするが、より重点的な取り組みとして、頻 度の高い老年症候群、すなわち転倒、失禁、低栄養、生 活体力低下、軽度の認知機能の障害やウツ、睡眠障害、 口腔内清潔と咀嚼能力の保持などについて、詳細な検査 によるスクリーニングを行なうことを目的としている。 具体的には、「お達者健診」は対象者を会場に招待して医 学的健康調査および面接聞き取り調査を実施している。 実際には私ども東京都老人総合研究所の所在する東京都 板橋区在住の70歳以上の高齢者を対象として毎年行なっ ている。受診者1人あたり1.5時間から2時間ですべての調査が終了するよう、会場内の安全と導線に配慮し、以下のような調査項目を含めている。

- (1) 身体計測(身長, 体重, 体脂肪)
- (2) 血圧测定(安静時,座位,2回測定)
- (3) 採血 (血算, 血清総コレステロール, 血清アルブ ミン等)
- (4) 心電図
- (5) 動脈硬化測定 (ABI, ba-PWV)
- (6) 骨密度測定 (DXA法による前腕骨密度測定)
- (7) 口腔内診察(咀嚼圧測定含む)
- (8) 身体機能(通常および最大歩行速度, 膝伸展力, 片脚起立時間, 手伸ばし試験, ペグボードテスト, 握力等)
- (9) 面接開き取り調査(個人属性,生活機能としてのADL, I-ADL,健康度自己評価,転倒,失禁,食品 摂取頻度調査,認知機能,うつ傾向,外出頻度,社 会参加状況等)

このような「お達者健診」により、例えば自立に対する認知機能の重要性や転倒に関しては約20%の者が最低1回は転倒し、転倒恐怖感が極めて大きな影響をもつこと、さらには、女性の場合約25%の者が失禁を経験しているなど、比較的元気に自立している(ように思われる)高齢者にも多くの潜在的問題が存在していることが明らかとなっている<sup>6-8</sup>。

「お遠者健診」によって、ハイリスク高齢者を抽出した後、転倒ハイリスク者に対しては「転倒予防教室」の6ヶ月間のプログラムによる下肢筋力を中心とした体づくりや、失禁経験者には3ヶ月間の骨盤底筋トレーニングを基本とした「失禁予防教室」に参加をうながしている。また低栄養(アルブミン値 $\le 3.9 \text{ g/dl}$ )の高齢者に対しては、地域で調理設備のある施設を利用し、「お遠者調理教室」を開催している。軽度の痴呆( $MMSE \le 23$ )の方々には痴呆予防の取り組みに参加して頂く、といったようなプログラムを用意し、少しでも老年症候群を抑制し、少しでも長く、健康長寿を目指す取り組みを展開している(図 1)。

今後の日本では、ますます少子高齢化が進展する。高齢者の健康度は今後も着実に向上してゆくものと推定されるが、しかし一方で後期高齢者を中心として加齢による身体機能の低下とそれに基づく生活機能の障害もまた増加すると考えられる。このような(超)高齢社会にあっては、高齢者の健康(寿命)の延伸とQOL向上に向けた新しいパラダイムが求められている。高齢者の自立を障害し要支援・要介護となる原因は疾病よりもむしろ著し

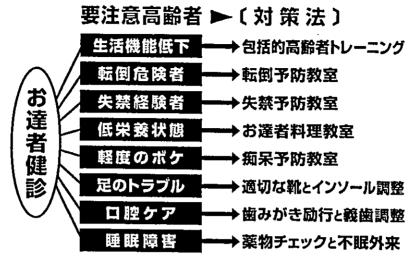


図1

く進行する虚弱と生活機能を障害する老年症候群が大きな要因であり、これに対する新しい対策と取り組みこそが、ますます重要になるものと考えられるのである。

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### 厚生労働科学研究費補助金

### 長寿科学総合研究事業

### 老化因子と加齢に伴う身体機能変化に関する 長期縦断的疫学研究

総 合 研 究 報 告 書 (平成14年度~16年度)

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主任研究者 下 方 浩 史 平成17年(2005年)3月

# Ⅲ. 研究成果の刊行物・別刷

#### ORIGINAL ARTICLE

## Current admission policies of long-term care facilities in Japan

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**Background:** The rapidly aging society in Japan is putting demands on long-term care facilities for the elderly who require care. In Europe and the USA, there is ongoing reform of elderly care services, but the establishment of system based on social insurance is still being explored in Japan.

Methods: Two studies were conducted, the first in 2000 and the second in 2001, involving 91 long-term care facilities located in or around the city of Nagoya. Questionnaires were sent to facility directors, chief administrators or head nurses to inquire about their admission policies for six major patient categories. Two educational lectures on methicil-lin-resistant Staphylococcus aureus (MRSA) and urinary incontinence were given between the distribution of the questionnaires.

Results: For all six categories featured on the questionnaire, the acceptance rate in both studies was the highest in geriatric hospitals, and an improvement in acceptance rates was seen in the second study in all three types of care facilities. When the effect the lectures had on changes in admission policies at these facilities was examined, no correlation was found.

Conclusions: Lectures should be given to facility management and personnel to raise their awareness of key issues and improve their efficiency.

Keywords: acceptance rates, admission policies, lectures, long-term care facility, MRSA.

#### Introduction

Japan has the fastest growing aging society in the world.<sup>1</sup> As with other developed countries, advanced medical technology has contributed to a considerable increase in life span and as a result, the number of elderly who require care has been increasing steadily, and the demand for institutional care is likely to intensify in the future. In Europe and North America, where a more gradual shift to an aging society has occurred, innovative elderly care services are being explored<sup>2</sup> and reforms

are ongoing. In April 2000, a public long-term care insurance system was introduced in Japan, and ways to establish an elderly care system based on social insurance were explored. Based on the 'Gold Plan' and 'New Gold Plan's formulated by the Health and Welfare Ministry, a reorganization of care facilities including nursing homes (NH), geriatric intermediate care facilities (GICF, which provide a certain amount of medical care), and geriatric hospitals (GH)4.5 was initiated. In order to improve facility standards and personnel placement, the two plans recommend the sharing of expertise by emphasizing more nursing care in nursing homes and more medical care in GICF and GH.2,5 However, reports have shown that the elderly do not systematically have access to institutional services3 because of an insufficient number of long-term care facilities3 and restrictive acceptance policies that limit the admission of carriers of methicillin-resistant Staphylococcus aureus (MRSA) and persons with other conditions.6-8

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It appears that admission to long-term care facilities is more frequently denied to the following types of patients: bacteria carriers, including MRSA carriers and Pseudomonas aeruginosa carriers, and persons requiring medical care, including nasogastric tube-feeding, persons requiring indwelling urinary catheter, persons requiring intermittent catheterization, patients with tracheostoma and patients who require intravenous hyperalimentation. Various studies have so far examined admission policies for MRSA carriers, 6,9 but very few have focused on other conditions. Therefore, we conducted two studies to examine the possible factors that prevent the admission of certain elderly patients into long-term care facilities. The first study was carried out in June 2000, immediately after the new public insurance plan was introduced, and the second in May 2001. In addition to MRSA status, we examined five other possible factors for admission refusals in long-term care

A general lack of knowledge among medical and welfare staff has been shown to be the primary factor for admission refusals of patients with MRSA infections<sup>7</sup> and the same holds true for elderly persons requiring a urinary catheter. Therefore, between the first and the second study, we gave two lectures to participating facilities, one on MRSA and one on urinary incontinence, in order to examine the effect of education on admission policies.

#### Methods

The study group comprised 91 long-term care facilities (35 NH, 40 GICH, 16 GH), all located within 20 km of the city of Nagoya. A telephone survey was conducted with either the director, chief administrator or head nurse of each facility and prior to the telephone survey, a questionnaire was sent to all facilities to inform them of the study. Some of the participants answered the questionnaire by mail, and we therefore did not need to telephone them.

The survey was carried out twice, once in June 2000, and later in May 2001. Using the same questionnaire on both occasions, we inquired about the facilities' admission policy for the following types of elderly patients: (1) MRSA carriers, (2) *P. aeruginosa* carriers, (3) nasogastric tube-fed persons, (4) gastrostomy tube-fed persons, (5) persons requiring an indwelling urinary catheter, and (6) persons requiring intermittent catheterization (Table 1). Additional questions about the admission policy for patients with a tracheostoma and patients requiring intravenous hyper alimentation were added to the questionnaire that was distributed to GH.

We categorized responses as 'possible' if the answer to whether or not the facility would admit someone with conditions attached. We categorized answers such as 'under consideration' or 'we would consider admission on a case by case basis' as 'others', and did not include

**Table 1** Questionnaire: The study on the current admission policy in the long term care facility. Please answer the following questions. Your answers will be gathered and analyzed statistically. Your privacy is strictly protected.

Acceptance of MRSA carriers 1. Possible 2. Impossible 3. Others ( 2 Acceptance of Pseudomonas aeruginosa carriers 1. Possible 2. Impossible 3. Others ( 3 Acceptance of nasogastric tube-fed persons 1. Possible 2. Impossible 3. Others ( 4 Acceptance of gastrostomy tube-fed persons 1. Possible 2. Impossible 3. Others ( 5 Acceptance of persons requiring an indwelling urinary catheter 1. Possible 2. Impossible 3. Others ( 6 Acceptance of persons receiving intermittent catheterization 1. Possible 2. Impossible 3. Others ( For the hospitals only Hospitalizing patients with a tracheostoma 1. Possible 2. Impossible 3. Others ( 8 Hospitalizing IVH 1. Possible 2. Impossible 3. Others (

Thank you very much for your cooperation. We will gather information by the phone at a later date.

these in our statistical analysis. In both studies, the acceptance rate was compared and examined among the NH, GICF, and GH for each question on the survey. In addition, we looked at the change in acceptance rates from 2000 to 2001 for each type of facility examined.

Between the distribution of the first and second questionnaire, lectures on MRSA and urinary incontinence were given to facility personnel, who attended these lectures voluntarily. We then categorized the facilities into two groups, a participating group, consisting of facilities whose personnel had attended the lectures, and a non-participating group (facilities where lectures had not been given). The lecture on MRSA focused mainly on general characteristics, pathogenicity, and infectivity. The lecture on urinary incontinence covered classification, causes, and means by which people adapt to having intermittent catheterization. The effect of the lectures was examined by comparing the pre- and postlecture acceptance rates.

Statview-J5.0 was used for analysis. Chi-squared test was used to compare the acceptance rates between three groups and between 2000 and 2001. Paired t-test was used to compare the acceptance rates between pre- and post lecture. The statistically significant difference was set at P < 0.05.

#### Results

In the study conducted in May 2000, 26 NH (74.3%), 34 GICF (85%), and 14 GH (87.5%) responded to our questionnaire, and in the second study on June 2001, 29 NH (82.9%), 35 GICF (87.5%), and 13 GH (81.3%) responded.

On whether they would admit MRSA carriers, in the first study, 8 NH (33%), 12 GICF (40%), and 7 GH (54%) replied 'possible', and in the second study, 9 NH (43%), 21 GICF (64%), and 7 GH (58%) gave that answer. In both studies, no statistically significant difference was found in the admission rates among the NH, GICF, and GH, despite the fact that acceptance rates in each facility did improve, as the second study results indicate (Fig. 1).

On whether they would accept *P. aeruginosa* carriers, in the first study, 8 NH (33%), 13 GICF (45%), and 8 GH (62%) responded 'possible', and in the second study, 13 NH (52%), 23 GICF (72%), and 8 GH (73%) replied 'possible'. In both studies, the GH showed the highest acceptance rate, followed by the GICF and NH, but no statistically significant difference was found among the facilities. Each type of facility improved their admission rate, as the second study results show, and a statistically significant difference was found in the GICF (P < 0.05) (Fig. 2).

On whether they would admit nasogastric tube-fed patients, in the first study, 12 NH (46%), 26 GICF (81%), and 13 GH (93%) answered 'possible', and in the second study, 16 NH (66%), 28 GICF (88%), and 12 GH (100%) responded 'possible'. In both studies, the GH had the highest acceptance rate, followed by the GICF and NH. In the first study, a statistically significant difference was found between the NH and GICF (P < 0.01), and in the second study, between the NH and GH (P < 0.05). Each type of facility improved their acceptance rate in the second

study, but no statistically significant difference was found (Fig. 3).

On whether they would accept gastrostomy tube-fed patients, in the first study, 12 NH (46%), 24 GICF (73%), and 13 GH (93%) replied 'possible', and in the second study, 16 NH (67%), 28 GICF (90%), and 13 GH (100%) answered 'possible'. Both studies revealed similar responses to the question of whether the facilities would admit nasogastric tube-fed patients. In the first study, a statistically significant difference was found between the NH and GICF (P < 0.05), and between the NH and GICF (P < 0.05), and between the NH and GICF (P < 0.05). Each type of facility showed an improvement in their acceptance rates in the second study, but no statistically significant difference was found (Fig. 4).

On whether they would accept patients requiring an indwelling urinary catheter, in the first study, 19 NH (73%), 29 GICF (88%), and 13 GH (93%) answered 'possible', and in the second study, 23 NH (92%), 32

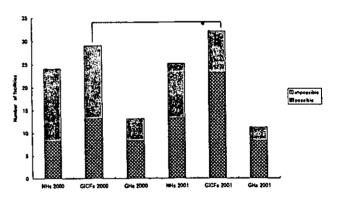


Figure 2 Admission policy for *Pseudomonas aeruginosa* carriers. Chi-squared test was performed to compare acceptance rates between 3 groups and between 2000 and 2001: \*P < 0.05.

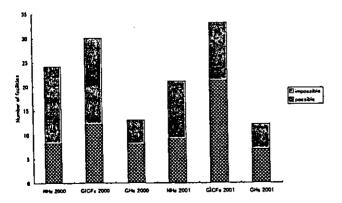


Figure 1 Admission policy for MRSA carriers. Chi-squared test was performed to compare acceptance rates between 3 groups and between 2000 and 2001. P value did not reach statistical significance.

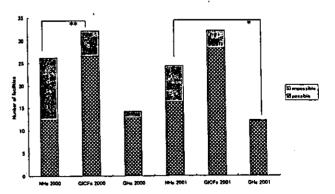


Figure 3 Admission policy for nasogastric tube-fed persons. Chi-squared test was performed to compare acceptance rates between 3 groups and between 2000 and 2001: \*P < 0.05, \*\*P < 0.01.

GICF (94%), and 13 GH (100%) responded 'possible'. As seen with the other responses, the acceptance rate was the highest in the GH, followed by the GICF and NH, but no statistically significant difference was found. Each type of facility showed an improvement in their acceptance rates in the second study, but no statistically significant difference was found (Fig. 5).

On whether they would admit patients requiring intermittent catheterization, in the first study, 15 NH (58%), 19 GICF (66%), and 12 GH (86%) replied 'possible', and in the second study, 12 NH (57%), 26 GICF (87%), and 10 GH (83%) answered 'possible'. The acceptance rates in each type of facility showed the same tendency as that observed for the question on the acceptance of patients requiring an indwelling urinary catheter, except for the difference between the GICF and GH that appeared in the second study. A statistically significant difference was found between the NH and GICF in the second study (P < 0.05). Each type of facility improved their acceptance rates in the second study,

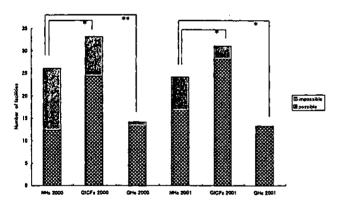


Figure 4 Admission policy for gastrostomy tube-fed persons. Chi-squared test was performed to compare acceptance rates between 3 groups and between 2000 and 2001: \*P < 0.05.

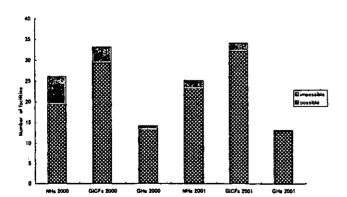


Figure 5 Admission policy for persons requiring an indwelling urinary catheter. Chi-squared test was performed to compare acceptance rates between 3 groups and between 2000 and 2001. P value did not reach the statistical significance.

but no statistically significant difference was found (Fig. 6).

The admission rate of NH for all six categories, in the first study, was found to be 33% for MRSA carriers as well as P. aeruginosa carriers, the lowest of all, and in the second study, 43%, again the lowest of all (Fig. 1). In both studies, a statistically significant difference was found between the admission rates for MRSA carriers and that for patients requiring an indwelling urinary catheter (P < 0.01). The lectures on MRSA were attended by 26 facilities (28.6%) and 28 (30.8%) attended those on urinary incontinence. In order to examine the effect of these lectures, we investigated only those facilities that had answered both questionnaires in 2000 and 2001, dividing them into participating and non-participating groups.

For the lecture on MRSA, we studied 61 facilities (20 in the participating group, 41 in the non-participating), and for the lecture on urinary incontinence, 61 facilities (18 in the participating group, and 43 in the non-participating). An improvement in the acceptance rates for MRSA carriers was observed in the second study, in both groups. A statistically significant difference was not found in the change of the acceptance rate in either group (Fig. 7).

For the lecture on urinary incontinence, the number of facilities in the-non-participating group that answered that it would be impossible for them to accept patients requiring intermittent catheterization decreased from 15 to 7, and the number of facilities that provided answers that we categorized as 'others' increased from 4 to 9. However, no statistically significant difference was found in either group (Fig. 8).

Finally, the responses to the questions added to the surveys distributed to the GH showed that 10 of 14 facilities deemed it 'possible' to accept patients with a tracheostoma, and 8 of 14 facilities considered it 'possible' to accept patients with intravenous alimentation

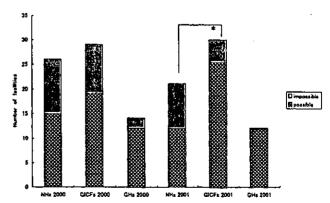
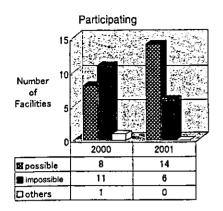


Figure 6 Admission policy for persons requiring intermittent catheterization. Chi-squared test was performed to compare acceptance rates between 3 groups and between 2000 and 2001: \*P < 0.05.



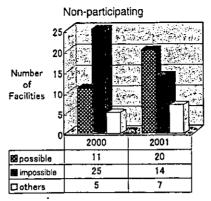
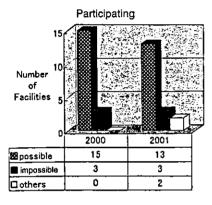


Figure 7 Effect of the lecture on MRSA on admission rates. The numbers are the sum of 3 groups. Paired *t*-test was performed to compare acceptance rates between 2000 and 2001. *P* value did not reach statistical significance.



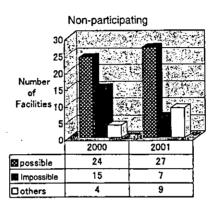


Figure 8 Effect of the lecture on urinary incontinence on admission rate. The numbers are the sum of 3 groups. Paired *t*-test was performed to compare acceptance rates between 2000 and 2001. *P* value did not reach statistical significance.

in the first study. In the second study, 9 of 13 facilities responded that it would be 'possible' for them to accept patients with a tracheostoma, and 8 of 13 facilities said that it would be 'possible' for them to accept patients with intravenous alimentation.

#### Discussion

The aim of this study was to clarify the admission policies that are currently in place in long-term care facilities by studying 91 such facilities (NH, GICF, and GH) in and around the city of Nagoya.

As possible factors affecting admission policies, we defined six categories: (1) MRSA carriers, (2) Pseudomonas aeruginosa carriers, (3) nasogastric tube-fed patients, (4) gastrostomy tube-fed patients, (5) patients requiring an indwelling urinary catheter, and (6) patients requiring intermittent catheterization.

With regards to MRSA carriers, a number of studies show a positive correlation between MRSA colonization and a higher death rate 6 months later. Other research, however, indicates that there is no clear causal relationship between MRSA colonization and infection in long-term care facilities. It has also been pointed out that infection and the prevalence of MRSA would not occur in long-term care facilities that practised strict isolation 6.11.12 because unlike hospitals, long-term care

facilities are rarely overcrowded with patients taking antibiotics,7 those with a central venous catheter13 and critically ill patients6 all of whom are considered to be the biggest carriers of this infection. Therefore, some studies have suggested that refusing admission to MRSA carriers into long-term care facilities is discriminatory. 6.14 In our study, the acceptance rate for MRSA carriers in NH was 33% in 2000, and 43% in 2001. The results obtained in a previous study by Washio and Fujishima,7 who reported that the acceptance rate for MRSA carriers was 33.3% in nursing homes, are consistent with our results. Although the acceptance rate for MRSA carriers in NH improved in the second study, it was still low in comparison with the other five categories, which suggests that refusing to admit MRSA carriers is an ingrained response by these facilities. The acceptance rate for P. aeruginosa carriers is also low in NH and the results indicate that patients who are carriers of other bacteria might be also dealt with unfairly. There is a pressing need for facility personnel to receive education on the nature and management of these conditions, and for further studies to be conducted.

The acceptance rate for nasogastric tube-fed patients, gastrostomy tube-fed patients, and patients requiring an indwelling urinary catheter were the highest in GH, followed by GICF and NH in both studies. GICF had a higher acceptance rate for patients requiring intermit-

tent catheterization than GH in 2001, but overall the rate was the highest in GH, followed by GICF and NH. Because all these conditions are categorized as requiring medical care, it seems appropriate that the highest acceptance rate was found in GH, where medical facilities, medical care and medically trained staff are more readily available than in GICF and NH. However, some reports have indicated that GH residents do not all require medical care, and that there are high medical demands in NH.5,15 Therefore, our results do not necessarily reflect the fairness and appropriateness of the admission policies we investigated. In addition, we did not ask the facilities whether or not they had sufficient staff to take care of additional residents, although a shortage of care staff may be one of the reasons why facilities claimed they were unable to accept new residents from the four categories chosen for the study. Because the shortage in human resources for geriatric care has long been recognized and studied,16 the government needs to examine its standards of human resource placement as a factor in limiting the admission of elderly who require care into long-term care facilities.

A comparison of the results from the two studies shows that, except for a decline in the acceptance rates for persons receiving intermittent catheterization seen in NH and GH, all of the facilities improved their acceptance rates for all patient categories. In particular, the acceptance rate for P. aeruginosa carriers in GICF in the second study showed a statistically significant difference. These improvements probably reflect the ongoing efforts made by these facilities to improve care. Other possible reasons are that, because of the introduction of the public long-term care insurance plan, senior citizens now have more choices of where to obtain care. Also, the expansion of care facilities has stimulated competition among them<sup>3,5</sup> and we assume that therefore longterm care facilities are concerned that their admission refusals could create a negative reputation among the elderly, of which there are many, still awaiting admittance into these facilities. 17,18 We did not investigate this issue in the present study, but expect to in the future.

The effect of the lectures on a change in admission policies was examined, but no correlation was found. We first assumed that lecture participants would mainly be care staff and decided that basic, practical information was appropriate for them. Thus, we focused on the general characteristics, pathogenicity, and infectivity of MRSA, and the classification, causes, and means by which people adapt to receiving intermittent catheterization for urinary incontinence. However, the lectures were mainly attended by chief administrators and directors, and not by the staff members who actually care for the elderly in these facilities. The content of the lectures might have been inappropriate; instead they should have been specifically aimed at encouraging admission. Yet another possible reason for the results obtained is

that both the participating and the non-participating groups already had some prior knowledge of these conditions. If that is the case, then public information or guidelines on admission policies may be needed, rather than knowledge. Further examination into the type of information that should be provided and the level of knowledge of participants is needed.

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#### ORIGINAL ARTICLE

# Factors associated with long hospital stay in geriatric wards in Japan

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**Background:** To reduce the length of stay (LOS) in hospital, the factors associated with extended LOS have to be identified.

Methods: A comprehensive geriatric assessment (CGA) of patients in a geriatric ward was carried out to identify the factors associated with LOS of more than 28 days.

Results: Of 193 patients (> 65 years old) who had been admitted to the geriatric ward of Nagoya University Hospital from home, 118 patients had complete CGA data sets. The CGA items were studied within 1 week of admission and analysis was performed by Chisquared followed by multilogistic analysis. Chi-squared analysis demonstrated that many of the basic activities of daily living (BADL) and instrumental ADL (IADL) had a significant association with longer LOS, but the contribution of psychological factors, assessed by mini-mental state examination and Geriatric Depression Scale-15, was relatively small. Multilogistic analysis showed that dependence on dressing assistance and medication assistance significantly increased the chance of having a LOS longer than 28 days.

Conclusion: Intervention to improve the ability to dress and take medication independently may reduce LOS.

Keywords: activities of daily living, comprehensive geriatric assessment, length of stay.

#### Introduction

In many countries including Japan, increasing medical costs are an urgent issue, and one of the main contributing factors is length of stay (LOS) in hospital. Patients in geriatric wards generally have a long LOS and reducing that time is one way of reducing medical costs, not necessarily only for administrative reasons, but also from the clinical point of view because unnecessarily long hospitalization may result in a decline of in the ability to perform activities of daily living (ADL) or contracting an infectious disease.

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Correspondence: Dr Hiroyuki Umegaki, Department of Geriatrics, Nagoya University Graduate School of Medicine, 65 Tsuruma-Cho, Showa-Ku, Nagoya, Aichi, 466-8550, Japan. Email: umegaki@tsuru.med.nagoya-u.ac.jp A comprehensive geriatric assessment (CGA) is a multidisciplinary diagnostic process that includes the medical, psychosocial, and functional aspects of the subject. CGA followed by therapy is called geriatric evaluation and management (GEM), which has been shown to be effective in several aspects including improved functional status, less placements in nursing homes, and improved diagnostic accuracy. 23

However, few studies have demonstrated the impact of GEM on LOS. One study in France showed that GEM reduced prolongation of LOS for non-medical reasons, but did not have a measurable impact on the duration of hospital stay. Collard et al. showed that in an acute care setting LOS was reduced and the total charge was lowered after GEM, although the effect was relatively limited.

To strengthen the impact of GEM on LOS, the factors associated with long LOS have to be identified and then more progressive intervention can be done.

#### Methods

#### Subjects

The study group were 289 elderly (> 65 years old) patients who were admitted to a geriatric ward between 1 September 1998 and 31 December 2000. Of these, 211 underwent CGA within 1 week of admission to hospital; CGA was not performed in 78 patients because of severe acute illness. Referral from another facility was the reason for admission for 18 patients and 193 were hospitalized from home. Complete CGA data sets were collected from 118 (50 males, 68 females) of the patients admitted from home.

#### CGA

For the CGA, we evaluated the basic activities of daily living (BADL), instrumental ADL (IADL), vision, hearing, and communication in the physical aspect, cognitive function and depression in the mental aspect, economic status, marital status, family status, relationship with family members, and ability to behave as a group in the social aspect.

#### BADL

The Barthel index was used to assess capability with BADL.<sup>6</sup> The total scores were divided between greater than or less than 16. In each item subjects were divided into two groups: the full mark and other.

#### **IADL**

The Lawton scale was used to assess IADL.<sup>7</sup> The total scores were divided between greater than or less than 4. In each item subjects were divided into two groups: the full mark and other.

#### Cognitive function

The mini-mental state examination (MMSE) was used to assess cognitive function.<sup>8</sup> The total scores were divided between greater than or less than 23. In each item subjects were divided into two groups: the full mark and other.

#### Depression

The Geriatric Depression Scale-15 was used to assess mood. The total scores were divided between greater than or less than 5.

#### Physical functional assessment

Vision, hearing, communication ability, and ability to ascend and descend stairs were evaluated by scoring

from 0 (unable) to 3 (able). In each item subjects were divided into two groups: the full mark and other.

#### Social status

Using scales developed by Ozawa<sup>1</sup> economic status family status, relationship with family, and group behav iour ability were assessed. Higher scores indicate a bet ter social life.

#### Statistical analysis

Statistical Analysis System (SAS) version 6.12 software was used for statistical analysis. Chi-squared analysis was performed in two groups: short LOS ( $\leq$  27 days) and long LOS ( $\geq$  28 days), followed by multiple logistic analysis. Fisher's exact probability test was used for comparing the binominal proportion from two independent samples in  $2 \times 2$  tables with small expected counts (less than 5).

In all analysis, P < 0.05 was considered statistically significant.

#### Results

Table 1 shows the characteristics of the patients and the relation of LOS assessed by single variant analysis is shown in Table 2. Chi-squared analysis showed that the total scores of BADL, IADL, vision, economic status, and group behaviour were significantly associated with longer LOS. Four disease categories (diabetes mellitus, cerebrovascular disease, ischemic heart disease, and dementia) that were relatively prevalent in the ward were not significant factors in the same analysis (data not shown). Tables 3–6 show the relation between each item of the BADL, IADL and MMSE. Independence of all BADL items, except grooming, was significantly associated with longer LOS (Table 3). Independence of all IADL items, except telephone use and travel, was significantly associated with longer LOS (Table 4). In the

Table 1 Characteristics of the subjects admitted to a geriatric ward

Age	$77.0 \pm 7.2$
M/F	50/68
Total score of BADL (mean ± SD)	$17.2 \pm 4.4$
Total score of IADL (mean ± SD)	$5.7 \pm 2.4$
Total score of MMSE (mean ± SD)	$25.8 \pm 4.7$
LOS (mean ± SD) (days)	$40.8 \pm 30.5$
No. of medications	$6.4 \pm 3.8$
No. of diseases	$3.4 \pm 2.0$

BADL, basic activities of daily living; IADL, instrumental ADL; LOS, length of hospital stay; MMSE, mini-mental state examination.

**Table 2** Relationship between length of stay (LOS) and gender, age and items from the Comprehensive Geriatric Assessment (CGA)

Item	LOS		<i>P</i> value	
	≤ 27 days	≥ 28 days		
Gender				
Male	22 (44.0%)	28 (56.0%)	NS	
Female	32 (47.1%)	36 (52.9%)		
Age (years)				
≥ 80	33 (44.0%)	42 (56.0%)	NS	
≤79	21 (48.8%)	22 (51.2%)		
Total BADL score				
≥16	49 (53.8%)	42 (46.2%)	< 0.001	
≤ 15	5 (18.5%)	22 (81.5%)		
Total IADL score	•			
≥ 4	49 (51.0%)	47 (49.0%)	0.02	
≤3	5 (22.7%)	17 (77.3%)		
Total MMSE acore	,			
≥ 23	45 (49.5%)	46 (50.5%)	NS	
≤ 22	9 (33.3%)	18 (66.7%)		
GDS-15	•			
≥5	25 (51.0%)	24 (49.0%)	NS	
 ≤ 4	29 (42.0%)	40 (58.0%)		
Vision	•			
Healthy	46 (51.1%)	44 (48.9%)	0.04	
Impaired	8 (28.6%)	20 (71.4%)		
Hearing	•			
Healthy	39 (45.3%)	47 (54.7%)	NS	
Impaired	15 (46.9%)	17 (53.1%)		
Communication	•			
Healthy	52 (48.1%)	56 (51.9%)	NS*	
Not healthy	2 (20.0%)	8 (80.0%)		
Economic status				
Independent	54 (48.2%)	58 (51.8%)	0.03*	
Dependent	0 (0.0%)	6 (100.0%)		
Marital status				
With spouse	25 (43.1%)	33 (56.9%)	NS	
Without spouse	29 (48.3%)	31 (51.7%)		
Familial status				
Not alone	43 (44.8%)	53 (55.2%)	NS	
Alone	11 (50.0%)	11 (50.0%)		
Familial relationships	•			
Intimate	28 (51.9%)	26 (48.1%)	NS	
Not intimate	26 (41.3%)	37 (58.7%)		
Group behaviour	•			
Eager to join	41 (55.4%)	33 (44.6%)	0.006	
Not eager to join	13 (29.5%)	31 (70.5%)		

<sup>\*</sup>Fisher's exact probability test.

MMSE, only 'calculation' showed statistical significance (Table 5). Five types of multiple logistic analyses were performed (Table 6). In model 1, items in the BADL scales (Barthel index) that had *P* values less than 0.10 in

the Chi-squared analysis were considered. Dressing showed a significantly high odds ratio. In model 2, items in the IADL (Lawton scale) that had P values less than 0.10 were considered. Dependence with laundry and

**Table 3** Relationship between length of stay (LOS) and items from the basic activities of daily living (BADL)

Item	LOS	LOS		
	≤27 days	≥ 28 days		
Fecal incontinence		<del> </del>		
Independent	50 (50.0%)	50 (50.0%)	0.04*	
Dependent	4 (22.2%)	14 (77.8%)		
Urinary incontinence		, ,		
Independent	48 (52.7%)	43 (47.3%)	0.005	
Dependent	6 (22.2%)	21 (77.8%)		
Grooming	` ,	, ,		
Independent	50 (46.7%)	57 (53.3%)	NS*	
Dependent	4 (36.4%)	7 (63.6%)		
Toileting	,	, ,		
Independent	50 (52.1%)	46 (47.9%)	0.004*	
Dependent	4 (18.2%)	18 (81.8%)		
Feeding	- (1070)	10 (0114,0)		
Independent	52 (49.1%)	54 (50.9%)	0.04*	
Dependent	2 (16.7%)	10 (83.3%)		
Transfer	_ (,	10 (33.2.13)		
Independent	48 (52.7%)	43 (47.3%)	0.002	
Dependent	5 (19.2%)	21 (80.8%)	0.002	
Walking	+ <b>(/</b>	(000000)		
Independent	46 (52.3%)	42 (47.7%)	0.02	
Dependent	8 (26.7%)	22 (73.3%)		
Dressing	, ,	(· /		
Independent	50 (53.8%)	43 (46.2%)	< 0.001*	
Dependent	4 (16.0%)	21 (84.0%)		
Stairs	, ,	<b>(</b> ,		
Independent	40 (55.6%)	32 (44.4%)	0.008	
Dependent	14 (30.4%)	32 (69.6%)		
Bathing	(/	()		
Independent	47 (54.7%)	39 (45.3%)	< 0.001	
Dependent	7 (21.9%)	25 (78.1%)		

<sup>\*</sup>Fisher's exact probability test

medication was significant. In model 3, items of calculation and copying a design, which had P values less than 0.10, were considered, and only calculation was significant. Model 4, in which every item that had a P value less than 0.10 was considered, showed that dressing and medication were significant. In model 5, items of physical function, social status and the total scores of both BADL and IADL, and MMSE were considered, and the total score of the BADL (Barthel index) was significant.

#### Discussion

The present study investigated the factors associated with long LOS. Single-variant analysis showed that the factors significantly associated with a LOS of more than

28 days were the total scores of both the BADL and IADL, the items of vision, economic status, and group behaviour.

Several studies have reported an association of LOS with ADL, <sup>10-15</sup> but not which items of the ADL are important for determining LOS. In the current study, Chi-squared analysis showed that all BADL items, except grooming, had a significant association with longer LOS. In multiple logistic analysis model 5, the total score of the ADL had the highest odds ratio, and within the ADL items (model 1) dressing was the factor most strongly associated with LOS. In model 4, in which all the items were considered, the item that had the strongest association was dressing. These results indicate that in the current study dependence of dressing had the most significant association with longer

**Table 4** Relationship between length of stay (LOS) and instrumental activities of daily living (IADL)

Item	LOS	LOS		
	≤ 27 days	≥ 28 days		
Telephone				
Independent	52 (47.3%)	58 (52.7%)	NS*	
Dependent	2 (25.0%)	6 (75.0%)		
Shopping				
Independent	42 (54.5%)	35 (45.5%)	P = 0.009	
Dependent	12 (29.3%)	29 (70.7%)		
Preparing meals				
Independent	27 (60.0%)	18 (40.0%)	P = 0.02	
Dependent	27 (37.0%)	46 (63.0%)		
Housework	•			
Independent	46 (52.9%)	41 (47.1%)	P = 0.009	
Dependent	8 (25.8%)	23 (74.2%)		
Laundry				
Independent	42 (56.8%)	32 (43.2%)	P = 0.002	
Dependent	12 (27.3%)	32 (72.7%)		
Travel				
Independent	52 (48.6%)	55 (51.4%)	$P = 0.06^{3}$	
Dependent	2 (18.2%)	9 (81.8%)		
Medication				
Independent	44 (56.4%)	34 (43.6%)	P < 0.00	
Dependent	10 (25.0%)	30 (75.0%)		
Money				
Independent	51 (50.0%)	51 (50.0%)	$P = 0.03^{4}$	
Dependent	3 (18.8%)	13 (81.3%)		

<sup>\*</sup>Fisher's exact probability test

LOS; however, the reason was not clear. Independence with dressing requires physical function as well as some aspects of judgment and therefore, the item of 'dressing' may represent a combination of several aspects of physical and mental function. Interestingly, intervention trials have shown an improvement in independent dressing 16.17 and a GEM approach stressing capability with dressing should reduce LOS.

Chi-squared analysis showed that all items in the IADL, except telephone use and travel, were significantly associated with longer LOS. Both multilogistic analysis model 2, in which IADL items were analysed, and analysis model 4 showed that needing assistance with medication significantly increased the chance of having longer LOS. Our previous study showed that patients who need medication assistance had significantly lower scores in ADL, IADL, and MMSE. Therefore, this item could also represent a combination of aspects. Issac *et al.* demonstrated that cognitive function strongly affected medication compliance in elderly patients. 19

Age and living status (living alone or not) were not significant factors. Epstein et al. showed that patients

of low socioeconomic status, including lower income, had longer hospital stays<sup>20</sup> and in the current study economic status was a significant factor in single variant analysis; however, multiple logistic analysis failed to show statistical significance. The current subjects were relatively wealthy and only 5% needed monetary assistance from relatives, whereas in the Epstein study 14% of the subjects had annual incomes less than US\$5000, which would affect the results of statistical analysis.

Incalzi et al. showed that extended hospital stay was significantly and independently predicted by polypharmacy and comorbidity, demonstrating that patients who were prescribed six or more medications and three or more diagnoses had significantly longer LOS.<sup>11</sup> In the current study, patients with six or more medications had longer LOS (43.9 vs 36.1 days), although it was not statistically significant, whereas the number of diseases did not have an impact on LOS.

The 4score, an index developed by Glass et al.,<sup>21</sup> defines four factors associated with longer LOS: (1) Is the patient 80 years old or more? (2) Will the patient have to live somewhere new at discharge? (3) Is there

Table 5 Relationship between length of stay (LOS) and items from the mini-mental state examination (MMSE)

Item	LOS		P value
	≤ 27 days	≥ 28 days	
Orientation (time)		<del></del>	
Fully	38 (51.4%)	36 (48.6%)	NS
Not fully	16 (36.4%)	28 (63.6%)	
Orientation (place)		·	
Fully	40 (48.2%)	43 (51.8%)	NS
Not fully	14 (40.0%)	21 (60.0%)	
Registration	, ,	, ,	
Fully	54 (46.2%)	63 (53.8%)	NS*
Not fully	0 (0.0%)	1 (100.0%)	
Calculation	` ,	, ,	
Fully	29 (58.0%)	21 (42.0%)	P = 0.02
Not fully	25 (36.8%)	43 (63.2%)	
Recall	( ,	(,	
Fully	33 (52.4%)	30 (47.6%)	NS
Not fully	21 (38.2%)	34 (61.8%)	
Language	, ,	<b>,</b> ,	
Fully	53 (45.7%)	63 (54.3%)	NS*
Not fully	1 (50.0%)	1 (50.0%)	
Repeat	. (	. ( 7	
Fully	50 (45.0%)	61 (55.0%)	NS*
Not fully	4 (57.1%)	3 (42.9%)	
Three-stage command	· · ·	, ,	
Fully	53 (46.1%)	62 (53.9%)	NS*
Not fully	1 (33.3%)	2 (66.7%)	
Read and obey	, -	. ,	
Fully	53 (46.5%)	61 (53.5%)	NS*
Not fully	1 (25.0%)	3 (75.0%)	
Write a sentence			
Fully	51 (47.2%)	57 (52.8%)	NS*
Not fully	3 (30.0%)	7 (70.0%)	
Copy a design	· · · · · · · · · · · · · · · · · · ·	, ,	
Fully	50 (49.5%)	51 (50.5%)	$P = 0.07^{4}$
Not fully	4 (23.5%)	13 (76.5%)	

<sup>\*</sup>Fisher's exact probability test

any disorientation? (4) If so, is the disorientation chronic? Two or more positive answers to these questions on admission increases the length of social stay in hospital. In the current study, neither the total score of the MMSE nor the item of 'orientation' was significantly associated with longer LOS. Age was not a significant factor, either. The disagreement could be explained by the different settings. The Glass study was done in an acute medical care ward, and in the current study the setting was a mixture of acute care and rehabilitation unit. Therefore, the factors associated with longer LOS may depend on the type of facility.

The current study was conducted in a geriatric ward in a university hospital and the patients had several particular characteristics compared with other hospitals in Japan. They were relatively wealthy<sup>18</sup> and many had a family member to live with (95 of 118 patients). Further analysis should be performed to confirm that the factors identified in the current study are significant in different settings.

In conclusion, in Japanese geriatric wards, dependence with the BADL, specifically dressing and taking medication, were the factors significantly associated with a LOS of more than 28 days.

Table 6 Multilogistic analysis of factors associated with longer length of stay (LOS)

<b>5</b>	,				
	Model 1	Model 2	Model 3	Model 4	Model 5
No. of patients	118	118	118	118	118
Vision				-	-
Economic status				-	
Group behavior				_	-
Total BADL score					5.1 (1.8:14.7)**
Fecal incontinence	<b>-</b> .				
Urinary incontinence	_			-	
Toileting	<del></del>			-	
Transfer	_				
Walking	_			_	
Dressing	6.1 (1.9:19.2)**			4.1 (1.2:13.6)*	
Stairs	_			-	
Bathing	_			-	
Total IADL score					-
Shopping		_		-	
Preparing meal		_		-	
Housework				-	
Laundry		2.5 (1.0:5.9)*			
Travel		-		<del></del>	
Medication		2.8 (1.1:6.9)*		2.6 (1.1 : 6.5)*	
Money		-		-	
Total MMSE score					
Calculation	•		2.4 (1.1:5.0)*	-	•
Copy a design			<u>-</u>		

In each model the variables were selected by step-wise method.

The variables that were analysed in each model, but not selected, are expressed by -.

The selected variables are expressed as odds ratio (95% confidence interval) and P value (\*P < 0.05, \*\*P < 0.01).

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#### **Brief Genetic Analysis**

# Association of Cholecystokinin 1 Receptor and $\beta_3$ -Adrenergic Receptor Polymorphisms with Midlife Weight Gain

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#### Abstract

KODA, MICHIKO, FUJIKO ANDO. NAOKIRA NIINO, HIROSHI SHIMOKATA. KYOKO MIYASAKA, AND AKIHIRO FUNAKOSHI. Association of cholecystokinin I receptor and  $\beta_3$ -adrenergic receptor polymorphisms with midlife weight gain. *Obes Res.* 2004;8:1212–1216.

We investigated the relationship of polymorphisms in the cholecystokinin 1 receptor [CCK1R; G to T (n-128), A to G (n-81)] and the  $\beta_3$ -adrenergic receptor ( $\beta_3$ -AR; Trp64Arg) with midlife weight gain. The participants were 1012 Japanese men and women (40 to 59 years of age). Their weight at 18 years old was obtained from a questionnaire. Weight change was defined as the current weight minus the weight at 18 years old. Subjects were grouped into four categories by these genotypes: W/W = noncarriers,  $W/H = Arg^{64}$ carriers of the  $\beta_3$ -AR, H/W = T (n-128) or G (n-81) carriers of the CCKIR, H/H = T (n-128) or G (n-81) and  $Arg^{64}$ carriers. In men, the interaction between the CCKIR and  $\beta_3$ -AR polymorphisms was significant (two-way ANOVA, p < 0.05), but neither the CCK1R nor the  $\beta_{3}$ -4R was individually associated with weight gain. The H/H group showed a higher possibility of weight gain of 10 kg or more compared with the W/W group in men. The odds ratio for weight gain (≥10 kg) of H/H was 2.54 (95% confidence interval: 1.50 to 4.30) compared with W/W. In women, neither main effect nor interaction was significant. These

results suggest that the combination of CCK1R and the  $\beta_3$ -AR polymorphisms is a contributing factor for midlife weight gain in men.

Key words: combination of polymorphism, body weight gain, middle-aged men

Age-related increases in body weight in young adult men and postmenopausal women have been reported. Weight gain is as harmful to the health as being overweight. In a previous study, weight gain from 20 years of age was closely associated with cardiovascular risk factors in middle-aged men (1), and weight gain from 18 years of age was associated with coronary heart disease risk in women (2). According to a Japanese national cross-sectional survey in 1999 (3), although the rate of excess weight (BMI  $\geq$  25 kg/m²) was 19.2% in those 20 to 29 years old, it increased to 29.6% in those 50 to 59 years old for men. In women, it was 7.3% in those 20 to 29 years old and 27.5% in those 50 to 59 years old.

There are several causes associated with weight gain, such as smoking, physical activity during leisure, alcohol consumption, and genetic factors (4-6). Regarding obesity, we reported the possibility that the polymorphism of the cholecystokinin 1 receptor (CCK1R)<sup>1</sup> gene may be related to an increase in body fat content in middle-aged and elderly people (7). Cholecystokinin (CCK) is a peptide hormone found in the central nervous system and gastrointestinal tract. CCK1R has been shown to mediate the CCK-induced suppression of food intake (8), and the peripheral administration of CCK1R antagonists increased food intake (9). However, Hamann et al. (10) found no evidence for its association with early-onset obesity in children and adolescents.

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<sup>&</sup>lt;sup>1</sup> Nonstandard abbreviations: CCKiR, cholecystokinin 1 receptor; CCK, cholecystokinin: β<sub>3</sub>-AR, β<sub>3</sub>-adrenergic receptor; NILS-LSA, National Institute for Longevity Sciences—Longitudinal Study of Aging.

The  $\beta_3$ -adrenergic receptor ( $\beta_3$ -AR) genotype has also been cited as a gene candidate related to obesity (6,11,12), and it is involved in the regulation of lipolysis and thermogenesis. Japanese (12), Pima Indians (6), and Alaskan Eskimos (13) have higher frequencies of the  $\beta_3$ -AR gene polymorphism than whites. However, some studies have suggested that the  $\beta_3$ -AR gene is not associated with obesity (13.14). Therefore, we investigated the relationship between CCKIR and  $\beta_TAR$  gene polymorphisms and weight gain from 18 years of age to middle age.

The means and SD of current weight, weight at 18 years, and weight change from 18 years by genotype are shown in Table 1. The means of weight change were 8.2 kg in men and 5.1 kg in women.

Genotype and polymorphism allele frequency distributions for CCKIR and  $\beta_3$ -AR are shown by gender in Table 2. These genotype frequencies were found to be in Hardy-Weinberg equilibrium in men and women. Gender differences in those frequency distributions were not significant. The frequency of the T (n-128) allele in CCK1R was 26% and that of the G (n-81) allele was ~40%. Funakoshi et al. (7) has found that there are two sequence changes in human CCKIR, a G to T change in n-128 and an A to G change in n-81. Six genotypes were identified as wild-type (G/G, A/A), heterozygote type (G/T, A/G), (G/G, A/G), (G/T, G/G), (G/G, G/G), and homozygote type (T/T, G/G). The genotype combinations G/T. A/A; T/T, A/G; and T/T, A/A were not found. On the other hand, the genotype frequency of the  $\beta_3$ -AR gene polymorphism is -33%, similar to previous studies in other Japanese (12).

Two-way ANOVA was carried out in which weight gain was taken as the dependent variable and the CCKIR and  $\beta_3$ -AR polymorphisms were independent variables. Neither CCKIR nor  $\beta_3$ -AR was individually associated with weight gain in men. However, the interaction between CCKIR and  $\beta_s$ -AR polymorphisms was significant (p < 0.05; Table 3). The main effects and the interaction were not significant in women.

Comparisons of the distributions of weight change from 18 years by genotype are shown in Table 4. Of the 564 men, 227 (40%) were noncarriers (W/W), 110 (20%) were Arg<sup>6</sup> carriers of the  $\beta_3$ -AR (W/H), 149 (26%) were T (n-128) or G (n-81) carriers of the CCKIR (H/W), and 78 (14%) were T (n-128) or G (n-81) and  $Arg^{64}$  carriers (H/H). Of the 548 women, 211 (38%) were W/W, 113 (21%) were W/H, 158 (29%) were H/W, and 66 (12%) were H/H. The frequency of weight gain (≥10 kg) was 40% for men and 24% for women. The distribution of weight change in men was different among the genotypes (p < 0.01). The frequency of a weight gain of ≥10 kg was higher in the H/H group than in the other three groups. The distribution in women was not different.

Finally, the risk of weight gain (≥10 kg) was estimated using multiple logistic regression analysis in men (Table 5).

Table 1. Characteristics of participants by gender

$154.1 \pm 4.9$
$54.1 \pm 8.0$
$48.9 \pm 6.0$
$5.1 \pm 7.7$
•

The odds ratio of the H/H group was significantly higher [2.54 (95% confidence interval: 1.50 to 4.30)] compared with that of the W/W group. However, in men with W/H or H/W, the odds ratios were not significant.

These results showed that the combination of CCK1R and  $\beta_3$ -AR polymorphisms was associated with a weight gain of ≥10 kg from 18 years of age in men. Hamann et al. (10) did not find that the CCK1R polymorphism was associated with early-onset obesity in children and adolescents. Although excess energy from increased food intake may be used for growth in a child, it is not usually used for growth in adults. After maturing, the polymorphism of the CCK1R gene may have an important role as a regulator of food intake.  $\beta_3$ -AR is involved in the regulation of lipolysis and thermogenesis. The resting metabolic rate in Arg64 homozygotes is significantly lower than in Trp64 homozygotes (15). Moreover,  $\beta_{s}$ -AR is expressed in visceral fat in humans (16), and visceral fat increases with advancing age (17). Therefore, in men carrying the T or G allele of the CCKIR and Arg<sup>64</sup> allele in  $\beta_3$ -AR, food intake may increase, but extra energy may not burn, leading to weight gain.

However, neither CCK1R nor  $\beta_TAR$  was individually associated with weight gain. CCKIR or  $\beta_3$ -AR alone was not likely to be a strong independent contributing factor of weight gain. Therefore, the results of the association between a single gene and weight gain in many previous studies have been contradictory. A combination of polymorphisms in two or more candidate genes may contribute to weight gain (e.g., the  $\beta_3$ -AR and uncoupling protein gene) (18,19). The simultaneous existence of two polymorphisms was associated with weight gain.

It remains unclear why these results were revealed only in men. For women, the physiological and environmental factors are relatively strong (e.g., pregnancy, parity, and menopause involve hormonal changes) (20). Furthermore, women may try more frequently to lose weight, and these factors may be stronger than genetic factors.

There are some limitations in this study. First, there may be other factors related to body weight. Smoking influences weight and weight change (4), and we, therefore, performed an analysis excluding smokers. The results were similar to

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