現在のインドネシアの高齢化率5%といえば、日本では1960年代のことであり、当時の日本に高齢者デイケアなどという概念が全く存在していなかったことを考えれば、高齢者に関する認識が着実に世界に広がりつつあることがうかがえよう。

ラオスにおける糖尿病

ラオスは東南アジアでも貧しい国で、2006年度の1人当たりの国内総生産は1,900米ドル(ちなみに日本は30,700米ドル)にすぎない。図3は、ラオスのサバナケット州ソンコン村在住の101歳の女性である。ラオスのような最貧国の郡部地域においても百寿者が出始めている。現代医療技術や防疫システムというグローバライゼーションの波は、経済成長の開始にほど遠いアジアの最貧開発途上国にまで確実に及んでおり、その平均寿命延長に成功していることがわかる。しかも驚いたことに、この百寿女性の血液検査を行ってみると、食後ではあるが血糖値が450mg/dLをスケールアウトしていた。治療はしていない。この女性に限らず、ラオスのこの地域には随時血糖値が高い例が多いことに気づき、翌年、約500名の60歳以上の高齢者に75gブドウ糖負荷試験を実施した。504名の対象者のうち、随時血糖値が110mg/dL以上の高齢者に再度呼びかけて負荷試験を行った結果、糖尿尿が17.7%、耐糖能異常が10.7%であった(図4)[2]。最近、やはりアジアの最貧国であるカンボジアでも、糖尿病の有病率が増加しているとする報告があり[3]、アジアにおける貧しい地域の糖尿病は国際公衆衛生上のあらたな課題となって注目されている。

高齢者のQOLとSpirituality

先進諸国であれ、発展途上国であれ、身寄りが少なく相対的に貧しい高齢者が入居できる老人ホームが制度化されている。

図3 ラオスにおける糖尿病をもった百寿者

日本では、「養護老人ホーム」がそれに該当し、入所条件は、入所時に歩行、更衣、摂食、トイレ、入浴などの身の回りの生活機能が自立しており、しかも市町村が相対的に貧しいと認定した高齢者のみが入所できる施設である。

一方、アジアの最貧国とされるミャンマーでも、同様に貧しく身寄りのない高齢者が入居できる仏教系、あるいはカトリック系の施設が存在する。日本と同様、入所条件は、基本的な日常生活機能が自立していて、身寄りが少なく貧しい高齢者で伝染性疾患をもたない高齢者とされている。

私たちは、ミャンマーの首都ヤンゴンにある仏教系とカトリック系のAged Poorが入所している高齢者のインタビューと診察結果をもとに、入所者のうつの頻度とQOLを評価し、同一の方法で評価した大阪の養護老人ホーム入所中の日本人高齢者と比較検討した。

高齢者では、身体的な問題とともに、気持ちが落ち込む“うつ”がしばしば認められる。日本の大阪にある養護老人ホームと、ミャンマーのカトリック系老人ホームならびに仏教系老人ホームに入所する老人のうつの頻度を比較すると、大阪の養護老人

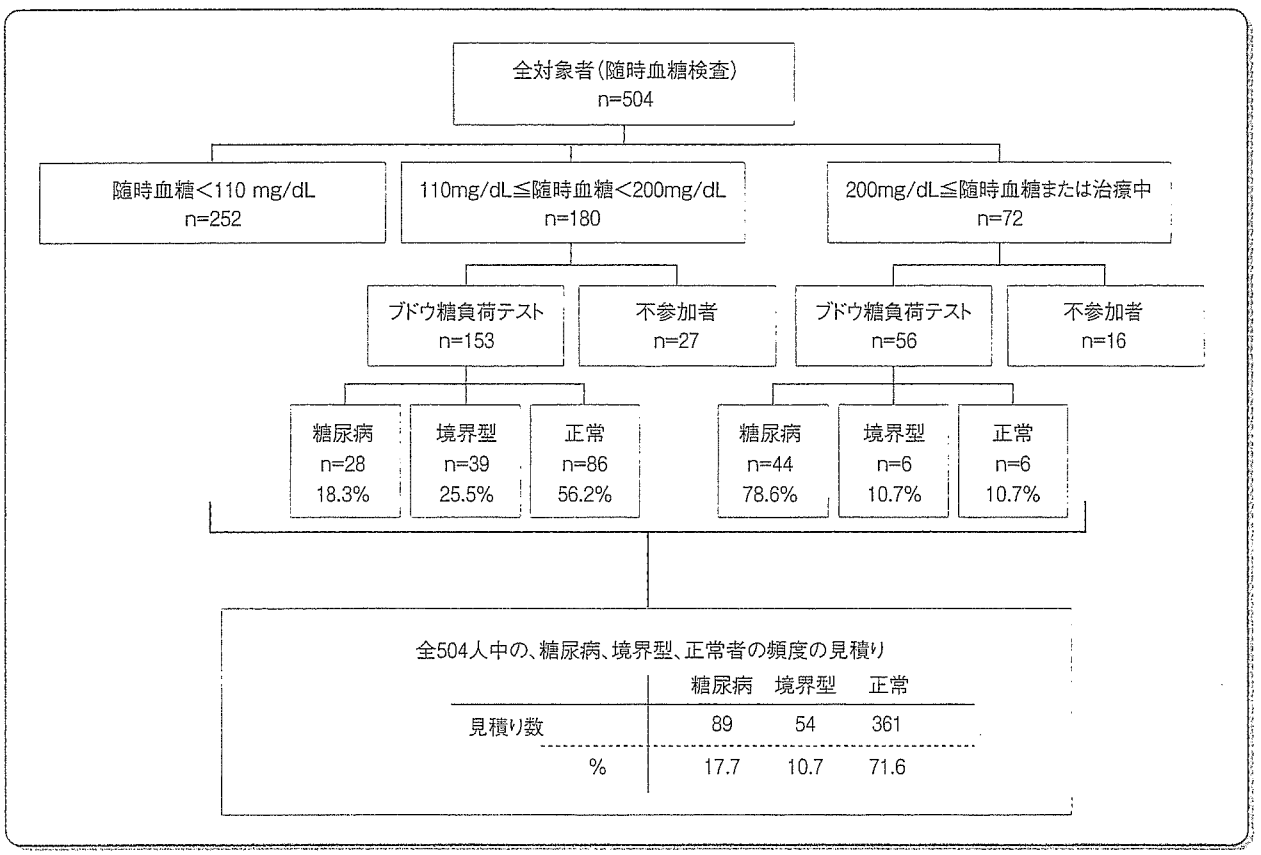

図4 ブドウ糖負荷テストによる、ラオス農村地域の糖尿病と境界型の頻度の見積り
[文献2)より改変して引用]

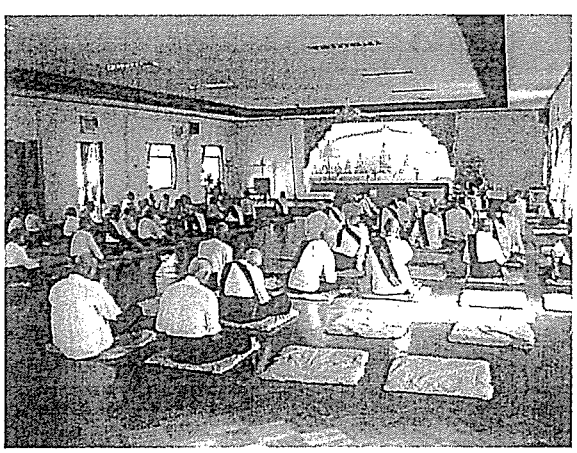

図5 ミャンマーの仏教系老人ホームにおける瞑想の時間

ホームでは、入所者の53%がうつを示すのに対して、ミャンマーのカトリック系老人ホームでは21%、仏教系の老人ホームでは6%であった。なぜ、貧しいミャンマーのなかでも特に貧しく身寄りのない高齢者の方が、豊かな日本で相対的に貧しい養護老人ホーム入所高齢者よりもうつが少ないのであろうか。

QOLやうつを規定する要因として、身体の状態、心理的要因、経済状態、社会的要因に加えてspiritual(霊的、精神的)な要素が重要とされている。ミャンマーの老人ホームに入所している高齢者に、最も幸せな時間はどういう時かと聞いてみると、仏教系ホームでは瞑想の時間(図5)、カトリック系ホームでは祈りや賛美歌の合唱、といった宗教的な

ふれあいをあげていた。特定の宗教をもたない日本人養護老人ホームに欠けているのは、このspiritualな要因ではないかと考えられる。

かつての日本人は、特定の宗教ではないとしても、自然崇拝や「孝」や「家」の価値概念、あるいは大和魂など、ある種spiritualな価値観をもっていた可能性が高いが、現在ではそれは失われている。個人の中には、それぞれspiritualな価値観があるのかもしれないが、まだ発見できていないように印象される。老年学の課題のひとつは、日本人高齢者の個人の中に潜在しているであろう多様なspiritualな価値観を探し出す手助けをすることでもあると思われる。

おわりに

日本の各地の横断調査のみならず、アジア諸国の高齢者の実態を調査してみて感じるのは、地域在住高齢者のADLやQOLに影響をもたらすのは、近代医療の質的レベルだけではなく、自然環境と文化背景であるように印象される[4]。現代医療の主たる場が病院であるのに対し、高齢者医療・介護の場は多くの場合、家庭であり地域である。その意味で、通常医療は臨床的であるが、高齢者医療・介護は臨地性(フィールド)が重視されなければならない。そして、人の老化現象にみられる普遍性と多様性の両面から高齢者をとらえきれたとき、21世紀の地球高齢社会に対する視野が開けてくるように思われる。

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ORIGINAL ARTICLE

Simple screening test for risk of falls in the elderly

Jiro Okochi,[1] Kenji Toba,[2] Tai Takahashi,[3] Kozo Matsubayashi,[4] Masanori Nishinaga,[5] Ryutaro Takahashi[6] and Takashi Ohrui[7]

[1]Hara-Doi Hospital, Japan Department of Clinical Research, Fukuoka, [2]Department of Geriatric Medicine, Kyorin University School of Medicine, Mitaka, [3]Department of Medicine and Welfare, International University of Medicine and Welfare, Otawara, [4]Center of South-east Asia, Kyoto University, Kyoto, [5]Department of Medicine and Geriatrics, Kochi Medical School, Kochi, [6]Tokyo Metropolitan Institute of Gerontology, Tokyo, and [7]Department of Geriatric Medicine, Tohoku University, Sendai, Japan

Background: The aim of this study is to construct a simple screening test for the risk of falls in community-dwelling elder persons.

Methods: A total of 1378 community-dwelling people aged 65 years and older in five different communities in Japan were asked to answer a self rated questionnaire including 22 items covering physical, cognitive, emotional and social aspects of functioning and environmental factors. At a six-month follow-up, the outcome of fall occurrence and the number of falls was ascertained by social workers, health visitors or nurses.

Results: Five out of 22 items were selected using a logistic regression model. Using this five-item version, a screening test was constructed, and at the best cut-off point, the sensitivity and specificity were 68% and 70%, respectively. The validity of this scale was tested on persons with cognitive dysfunction.

Conclusion: The simplicity and the predictive validity of the screening test support the use of this test in health check ups or general outpatient facilities.

Keywords: accidental fall, aged, mass screening, reliability and validity, risk factor.

Introduction

Falls are rated as the third leading cause of a bed-ridden state and are among the principal causes of morbidity in the elderly in Japan.[1] Previous studies evaluating the risk factors for falls have used history of falls, results of physical performance tests,[2] activity of daily living (ADL)[2,3] and balance and gait[4] as predictors.

Early identification of falls risk is likely to result in earlier implementation of interventions and to minimize development of unwanted sequels such as reduced confidence and activity levels.[5]

In Japan, the Ministry of Health, Labour and Welfare has put roughly 6000 local home care support centers around Japan. The task of these centers, according to Long-Term Care Insurance for the elderly, includes screening of the elders at risk of developing disabilities, including risk for falls. In this context, it is critical to develop a simple screening test to adequately evaluate the risk of falls for each elderly person.

The aim of this study is to evaluate predictive validity of a simple questionnaire composed of 22 items, with the intention of constructing a shortened version that would be simple, but effective to assess the future risk of falls during periodic health check-up or outpatient visits.

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Correspondence: Dr Jiro Okochi, Hara-Doi Hospital, 6-4-8 Aoba, Higashi-ku, Fukuoka 813-8588, Japan. Email: pxu14045@nifty.com

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All elderly persons who participated in this research gave written informed consent.

Methods

The initial 22-item questionnaire was constructed by the Working Group of Fall Prevention commissioned by the Japanese Ministry of Health, Labour and Welfare. Known risk factors are transformed into comprehensible text for the elderly, as shown in Table 1. These items were selected by studying both international and Japanese research articles on fall risk factors.[6]

The interclass coefficient (ICC) of the one month test-retest reproducibility study of the 22-item questionnaire score was satisfactory (ICC 0.74, 95% CI 0.46–0.89, $n = 21$).[6]

Individuals chosen for this study lived in five different urban and rural communities and they were over 65 years old.

In cases where subjects had cognitive impairment or difficulty answering, a family member acted as a proxy to help answer the questionnaire.

The outcome of fall occurrence and the number of falls were confirmed by social workers, health visitors or nurses six months after baseline measurement. A fall was defined as an unintentional change in position resulting in coming to rest on the ground or other lower positions.[3]

Statistical analysis was performed on subjects who completed the questionnaire both at baseline and at six month follow-up. One half of the subjects were randomly selected, and the relationship between falls and potential predictors was examined by χ^2 test for each predictor separately (developing samples). Items that achieved statistical significance of $P < 0.05$ were incorporated in the logistic regression analysis to identify predictors. Then, the questionnaire items considered to be associated with falls were selected using any falls as an outcome variable, by forward stepwise selection by the logistic regression model ($P < 0.05$).

The predictive power of the set of selected items, adjusted by the odds ratio, was determined using the area under the Receiver-Operating Characteristic (ROC) curve (AUC) on the other half of the subjects as the validating sample. Finally, the sensitivity and specificity of the model were calculated to obtain the cut-off point.

To test the validity of the scale on persons with cognitive dysfunction, different item functioning (DIF) analysis was performed on subgroups with and without cognitive dysfunction using the Rasch measurement

Table 1 The initial 22-item questionnaire constructed by the Working Group of Fall Prevention and commissioned by the Japanese Ministry of Health, Labour and Welfare

Questionnaire items	Answer (%)†	Incidence of fall (%)‡	*P*
Q1. History of fall within one year = yes	107 (16%)	54 (50%)	$P < 0.0001$
Q2. History of stumbling within one year = yes	288 (42%)	75 (42%)	$P < 0.0001$
Q3. Can you climb stairs without help? = no	261 (38%)	65 (25%)	$P = 0.0001$
Q4. Do you feel your walking speed declined recently? = yes	353 (51%)	76 (22%)	$P = 0.0025$
Q5. Can you cross the road within the green signal interval? = no	74 (11%)	25 (11%)	$P = 0.0019$
Q6. Can you walk 1 km continuously? = no	172 (25%)	46 (27%)	$P = 0.0011$
Q7. Can you stand on one foot for about five seconds? = no	180 (26%)	55 (31%)	$P < 0.0001$
Q8. Do you use cane when you walk? = yes	123 (18%)	43 (35%)	$P < 0.0001$
Q9. Can you squeeze the towel tightly? = no	80 (12%)	26 (33%)	$P = 0.0026$
Q10. Do you feel dizzy? = yes	151 (22%)	39 (26%)	$P = 0.0076$
Q11. Is your back bended? = yes	213 (31%)	62 (29%)	$P < 0.0001$
Q12. Do you have knee pain? = yes	264 (38%)	64 (24%)	$P = 0.0005$
Q13. Do you have a vision problem? = yes	292 (42%)	56 (19%)	$P = 0.2794$
Q14. Do you have a hearing problem? = yes	227 (33%)	48 (21%)	$P = 0.0781$
Q15. Do you think you are forgetful? = yes	332 (48%)	73 (22%)	$P = 0.0020$
Q16. Do you feel anxious to fall when you walk? = yes	226 (33%)	60 (27%)	$P = 0.0001$
Q17. Do you take more than five kinds of prescribed medicines? = yes	161 (23%)	39 (24%)	$P = 0.0231$
Q18. Do you feel dark walking within your home? = yes	54 (8%)	18 (33%)	$P = 0.0124$
Q19. Are there any obstacles within the house? = yes	87 (13%)	25 (29%)	$P = 0.0181$
Q20. Is there any level difference within your home? = yes	426 (62%)	79 (19%)	$P = 0.1799$
Q21. Do you have to use stairs in daily living? = yes	129 (19%)	23 (18%)	$P = 0.7951$
Q22. Do you walk steep slope around the house? = yes	202 (29%)	28 (14%)	$P = 0.2517$

†The answers as indicated in the question raw. ‡The incidence of fall among the relevant answer.

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technique.[7–9] Three hundred persons were randomly selected to obtain adequate sample size for this analysis.[10]

In addition, results of the ROC curve were stratified by the presence and absence of memory problem using Q15 of the questionnaire to test the validity of the short version on those with cognitive function problems.

Results

Of 1734 elderly, 1378 (79%) completed the questionnaire both at the baseline study and its six month follow-up. The mean age of the subjects was 75.8 (SD 6.8) years. The number of elders by five research centers was, 1050, 104, 82, 81 and 61, respectively. At least one fall had occurred in 208 elderly (15.1%) during the six month follow-up period. Of these, 103 (50%) suffered from multiple falls, ranging in number from 2 to 20.

Of eligible samples, 1026 elders provided information regarding mobility, cognitive status and ADL regarding eating and toileting. In mobility, no disability was seen in 69.8% of them, while mild difficulty in climbing stairs was present in 18.1%, and moderate or severe difficulty required cane or wheel chair for moving around outside in 12.1%.

In cognitive status, no memory disturbance was seen in 62.8%, while mild and severe memory dysfunctions were in 26.0% and 8.0%, respectively.

Regarding eating ADL, 93.4% showed no problem, while 4.6% complained they had a mild problem, and 2.0% required assistance. Toileting related ADL was intact in 89.0% of the elders while mild difficulty and dependent status on toileting were seen in 6.0% and 5.0%, respectively. Although 8.3% of them were living alone, 23.0% were with their spouse, and the rest were with their children.

The samples were then divided into the developing samples ($n = 689$) and validating samples ($n = 689$). There was no statistical significance between these two samples, in distribution of living areas, gender and response pattern to the questionnaire items examined by χ^2 test (data not shown). The average age of the validating samples (75.8) was not significantly different from developing samples (75.7) by t-test.

Table 1 shows the predictors in relation to falls in developing samples. The incidence of at least a single fall and multiple falls were 108 (15.7%) and 55 (8.0%), respectively. Gender did not achieve the statistical significance to single fall ($P = 0.05$) and multiple falls ($P = 0.15$), respectively. Fallers were elder than non-fallers ($P < 0.01$) with average age of 79.1 versus 75.8, respectively.

Questionnaire items, except for Q13, Q14, Q20, Q21 and Q22, achieved statistical significance and were entered into the regression model. Table 2 shows the item selected by the stepwise logistic regression model.

Using the odds ratio at integer level as the weight of these five items, we constructed a screening test whose score ranged from 0 to 14, and the AUC was 74% (95% CI 69–79%) in the validating samples, as shown in Figure 1. This was at the same level as the AUC of initial 22 items score (72%:95% CI 67–79%)

The maximum sum of sensitivity and specificity reached <6 (sensitivity 0.68, specificity 0.70) and <7 (sensitivity 0.67, specificity 0.71). If a cut-off score of <6 was applied, subjects identified as positive had a 27.9% rate of falls (positive predictive value) compared with a

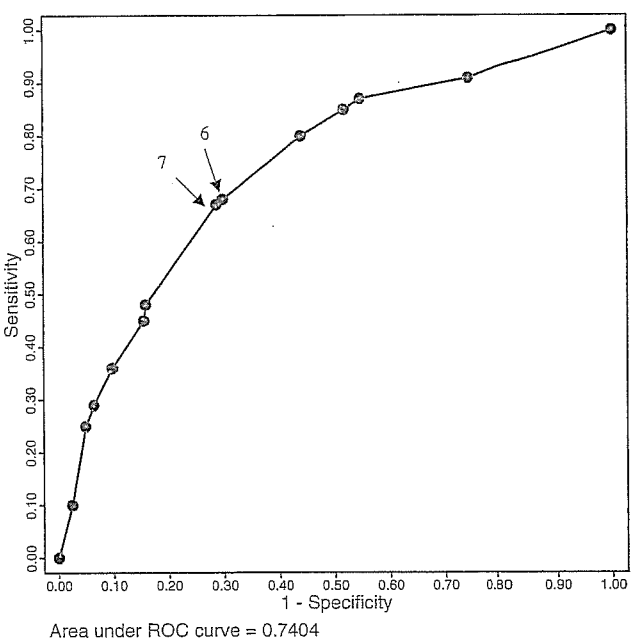

Figure 1 The Receiver-Operating Characteristic (ROC) of the five-item screening test to detect elderly persons at risk of falling.

Table 2 Questionnaire items selected by the stepwise logistic regression model

Questionnaire item selected by step wise logistic regression model	Odds ratio	95%CI	P
Q1. History of fall within one year = yes	4.5	(2.8–7.2)	0.00
Q4. Do you feel your walking speed declined recently? = yes	1.9	(1.0–3.6)	0.04
Q8. Do you use cane when you walk? = yes	1.8	(1.1–2.8)	0.02
Q11. Is your back bended? = yes	1.8	(1.1–2.8)	0.02
Q17. Do you take more than five kinds of prescribed medicines? = yes	1.7	(1.0–2.7)	0.03

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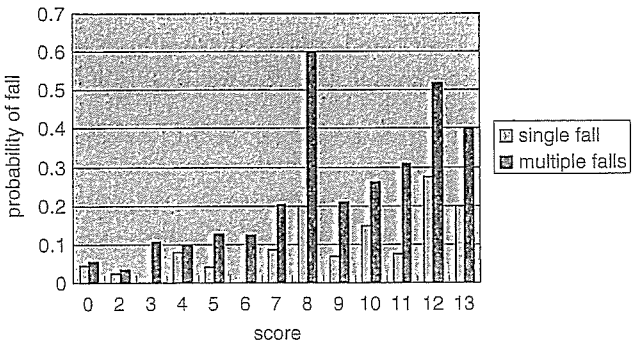

Figure 2 The probability of single and multiple falls by score.

7.2% rate in negative individuals (negative predictive power: 93%), with an odds ratio of 3.88 (95% CI 3.16–4.75).

The sensitivity and specificity was 0.63 and 0.67, respectively, for multiple falls. The positive and negative predictive value at this cut off score for multiple falls was 0.12 and 0.96, respectively, with the odds ratio of 3.04. Figure 2 illustrates the probability of fall by score levels.

On Rasch analysis of each item, some items did not fit the Rasch Model (Q16, Q20, Q21 and Q22) and these items were deleted for subsequent DIF analysis. Then no item showed DIF on cognitive functioning after Bonferroni adjustment (data not shown). After stratifying the sample with Q15, the area under ROC curve was 0.74 (95% CI 0.66–0.82) and 0.74 (0.69–0.78) for with and without cognitive dysfunction, respectively.

Discussion

Falls are considered as having multiple risk factors.[11] Previous epidemiological studies have identified the risk for falls, for example, history of falls,[2,3,12–15] activity of daily living (ADL),[2,3,15] cognitive and sensory function,[2,3,12,15] chronic conditions,[12,16,17] and medication use.[3,16–19]

Many studies tried to convert these risk factors for fall risk screening.[3,4,20] These screening tools for elders have been developed for various care settings, including residential,[14,21] intermediate[22] and inpatient care[23–25] as well as for community.[26–28]

Initially, the authors selected a comprehensive questionnaire composed of 22 items that can be answered by yes or no, and then selected several items that can be applied for mass screening or in general practice settings[6] because of the requirement of Japanese long-term care insurance (LTCI) law.

The items selected by the logistic model in this study were history of falls, walking speed, cane use, back deformation and medication use. All of these items were in concordance with the previous reports.

We also included environmental factors as part of the questionnaire. On comparison between fallers and non-fallers, environmental barriers such as level difference, stair and slope were not identified as risk factors, indicating the barrier recognized by the elders may not be associated with falls. All other items, except for vision problems were associated with incidence of falls.

The use of large prospective validating samples adds strength to this study. In most similar studies, the predictive validity is tested only on the developmental sample of the tools, and thus the predictive performance in a new sample is expected to be optimistic.[29] Although the predictive power on the development sample is usually high, the predictive power is usually lower in the validating samples.[30] In addition, the sensitivity of the scale is lower in the validating sample[31] and only a few studies use a large scale validating sample as was used in this study.[26]

Finally, the AUC of the initial 22 items were at the same level of the shortened five-item version. Therefore, the shortened version is preferred for its simplicity. In addition, the five-item scale was validated on the elderly with and without problems of cognitive function.

In the process of item selection using the logistic regression, inclusion criteria were $P < 0.05$, and exclusion criteria were $P > 0.10$. This procedure resulted in inclusion of items with weak association, such as Q4 and Q17. However, the adequacy of including these two items was proved on the validating sample.

In validating samples, the negative predictive value was 0.92 for single falls and 0.96 for multiple falls indicating that those with negative result have very low risk of falling in the next six months. This property of the high negative predictive validity makes the use of the screening test useful in mass screening.

History of fall was one of the most frequently reported risk factor of falls.[32,33] Decline of walking speed was captured with other questionnaire studies, as well as by physiological measurement.[6,18,34] Cane users and kolioskiphosis might have relation to bone abnormalities such as osteoporosis or arthritis.[13] These Q4, Q8 and Q11 compose a spectrum of physiologic decline referred to as frailty.[35,36] The relationship between medication use and falls can be explained by the effects of a drug itself that might cause sensory and balance disturbance, and also decreased metabolism, which relates to the loss of physiologic and metabolic function. Medication review is a possible intervention to prevent falls.[37]

In conclusion, a simple screening tool for falls is constructed using a large scale developing and validating sample. The scale constructed in this study is simple and valid. Therefore, it can be used as a screening tool of falls for community-dwelling elders.

Acknowledgment

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Original Article

High Morning Home Blood Pressure Is Associated with a Loss of Functional Independence in the Community-Dwelling Elderly Aged 75 Years or Older

Masanori NISHINAGA, Jun TAKATA, Kiyohito OKUMIYA*, Kozo MATSUBAYASHI**, Toshio OZAWA***, and Yoshinori DOI

To elucidate the relationship between home systolic blood pressure (SBP) and functional impairment in the elderly 75 years or older, 461 community-dwelling subjects (192 men, 269 women, mean age: 80 years) were studied. Home blood pressure was measured twice in the morning and twice in the evening for 5 consecutive days with an automatic cuff-oscillometric device. Total/high-density lipoprotein cholesterol and several functional assessments were evaluated. A subject was determined to exhibit a loss of independence according to the activities of daily living (ADL) score in a study conducted in 2001. Based on the mean home SBPs (mSBP) and morning–evening SBP differences (dSBP), the subjects were classified into 4 groups as follows: hypertensive/morning-dominant (HM; mSBP≥135 mmHg, dSBP≥15 mmHg), hypertensive/sustained (HS; mSBP≥135 mmHg, dSBP<15 mmHg), normotensive/morning-dominant (NM; mSBP<135 mmHg, dSBP≥15 mmHg), and normotensive/controlled (NC; mSBP<135 mmHg, dSBP<15 mmHg). There were no differences in sex, cholesterol levels, history of stroke, other cardiovascular diseases (CVDs), and cognitive function, but there were significant differences in age, antihypertensive medications, the neurobehavioral test scores, and ADL scores. There were no significant differences in terms of mortality and CVD events. In the survivors, HM and HS were independent risk factors for a loss of independence, after adjustments were made for onset of stroke, age, antihypertensive therapy, history of CVD, as well as neurobehavioral test scores and ADL scores (odds ratio [OR]: 12.2 and 3.78, respectively). After the same adjustments as those mentioned above were made, HM and HS were found to be negative determinants of survival and maintenance of independence (OR: 0.082, 0.270, respectively). In conclusion, high home SBP (≥135 mmHg) and high dSBP (≥15 mmHg) were found to be important in determining the levels of disability for the very elderly. (*Hypertens Res* 2005; 28: 657–663)

Key Words: home blood pressure, elderly, morning hypertension, independence, successful aging

Introduction

Recently there have been rapid increases in both the population and life span of the elderly in developed countries, which has resulted in a considerable increase in the number of frail elderly people. "The project to reduce the number of dependent elderly persons" has been promoted as an important

From the Department of Medicine and Geriatrics, Kochi Medical School, Kochi, Japan; *Research Institute for Humanity and Nature, Kyoto, Japan; **South-East Asia Research Center, Kyoto University, Kyoto, Japan; and ***Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan.

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Address for Reprints: Masanori Nishinaga, M.D., Ph D., Department of Medicine and Geriatrics, Kochi Medical School, Kohasu, Oko-cho, Nankoku 783–8505, Japan. E-mail: nishinam@med.kochi-u.ac.jp

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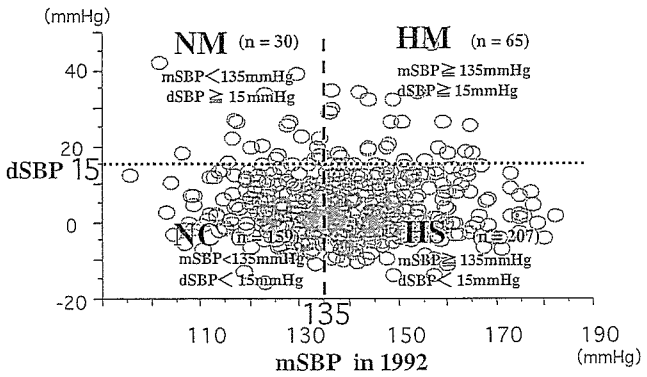

Fig. 1. *Classification of four groups according to the distribution of mean home SBP (mSBP) and morning–evening home SBP differences (dSBP). HM, hypertensive/morning-dominant; HS, hypertensive/sustained; NM, normotensive/morning-dominant; NC, normotensive/controlled.*

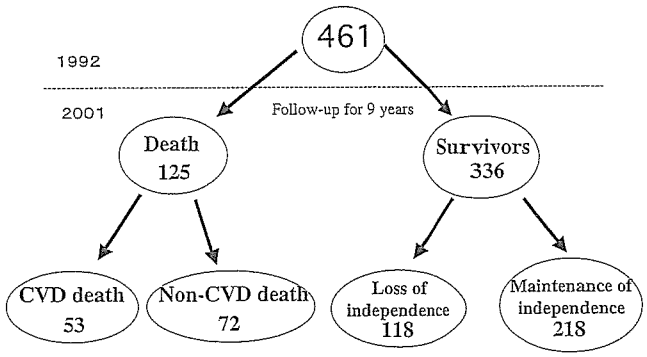

Fig. 2. *Outcome after a 9-year follow-up period. CVD, cardiovascular disease, including stroke.*

issue not only from the medical, but also from the socioeconomic point of view. This project should be considered a top priority, and appropriate measures should be taken to improve the current situation (*1*). Although stroke is a major cause of mortality and disability in the elderly (*2–4*), the management of hypertension in the community has contributed to an outstanding reduction in the incidence of stroke (*5*, *6*).

In many previous epidemiological studies on blood pressure (BP) in the elderly, the mortality and morbidity associated with stroke and other cardiovascular diseases (CVDs) have been selected as the endpoint (*7–9*). There have been also several epidemiological studies of the relationship between hypertension and dementia (*10*, *11*). However, assessments of functional abilities, the most important factor for elderly persons and their caregivers, have been rarely conducted.

Improving the management of BP for the prevention of stroke and other CVDs has led to the popularization of home BP monitoring devices among the general public (*12*, *13*). However, there have been few reports concerning home BP values in the elderly. Increased BP in the morning is considered as a strong risk factor for stroke and other CVDs (*14–17*). It remains to be clarified whether such an elevation in BP in the morning is also a risk factor for a loss of functional independence in the elderly.

In the present study, we recruited community-dwelling elderly people 75 years of age or older, and conducted medical and functional assessments. We followed the subjects for 9 years. The purpose of our study was to clarify the relationship between home BP values and functional disabilities, as well as that between home BP and the mortality/incidence of stroke. Furthermore, we studied morning–evening home BP differences in this very elderly sample.

Methods

Subjects

The study subjects were elderly people, aged 75 years or older, who resided in Kahoku Town, Kochi Prefecture, Japan in 1992. All subjects applied to participate in the home BP monitoring program. Subjects with atrial fibrillation were excluded because of the potential inaccuracy of their home BP measurements. A total of 461 people were recruited as the subjects of our study (192 men, 269 women, mean age: 81 years).

Home BP Measurement

Home BP was measured in 1992 with an automatic device (HEM-755C; OMRON Life Science Co., Ltd., Kyoto, Japan) based on the cuff-oscillometric method. The validity of BP measurement according to this method has been reported in several studies (*18–20*). The subjects and their caregivers were taught by community nurses how to measure the BP at home using this device. According to a previously reported method (*21*), BP was measured in the non-dominant arm after taking at least a 5-min rest in a sitting position, twice in the morning (6–7 AM) and twice in the evening (8–9 PM), for 5 consecutive weekdays.

We obtained the data regarding the total mean systolic BP (mSBP), morning and evening systolic BP (SBP), morning and evening diastolic BP (DBP) and pulse rates (PR). The mean morning–evening SBP differences (dSBP) were calculated. We defined subjects with mSBP≥135 mmHg as hypertensive or poorly controlled subjects, according to the Japanese Society of Hypertension (JSH) Guidelines for the Self-Monitoring of Blood Pressure at Home (*12*). We also divided our subjects into two groups by using mean+1SD of the dSBP. There were no subjects whose mean DBP values alone exceeded 85 mmHg.

Table 1. Basic Characteristics (1992)

	NC (n=159)	NM (n=30)	HS (n=207)	HM (n=65)
Age (years)*	80.3±4.5	81.5±5.1	80.5±5.1	81.4±5.3
Men (n [%])	74 (46.5)	13 (43.3)	79 (38.1)	26 (40.0)
SBP (mmHg)**	125±8	124±8	148±11	150±10
DBP (mmHg)**	72±7	73±9	80±11	81±9
PR(/min)*	68±8	67±7	69±8	68±12
Morning SBP (mmHg)**	126±9	135±9	149±12	162±11
Evening SBP (mmHg)**	123±9	113±9	148±12	138±11
Total cholesterol (mg/dl)	190±35	210±39	186±38	195±42
HDL cholesterol (mg/dl)	48±14	56±10	45±13	44±12
ADL (full score: 21)	20.4±1.9	20.8±0.8	20.2±2.6	20.2±1.9
MMSE (full score: 30)	27.2±4.4	28.4±2.2	27.3±3.2	27.5±3.2
Up and Go test (s)	13.0±3.2	13.0±2.8	14.1±4.6	14.9±5.4
Antihypertensive drugs** (Yes, n [%])	38 (23.9)	10 (33.3)	89 (43.0)	40 (61.5)
History of CVD (Yes, n [%])	16 (10.0)	1 (3.3)	13 (6.3)	4 (8.1)

NC, normotensive/controlled; NM, normotensive/morning-dominant; HS, hypertensive/sustained; HM, hypertensive/morning-dominant; SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse rate; HDL, high-density lipoprotein; ADL, activities of daily living; MMSE, mini-mental state examination; CVD, cardiovascular disease, including stroke. *ANOVA, $p<0.05$, **ANOVA, $p<0.01$.

Annual Self-Administered Questionnaire

In the baseline survey (1992), the self-administered questionnaire was addressed to the study subjects to obtain information about characteristics potentially related to their BP, mortality, and disability; the data collected included a history of stroke, heart disease, and bone disease or arthropathy, antihypertensive medications, current and past cigarette smoking, current intake of alcohol, and activities of daily living (ADL). All of the response sheets submitted by the subjects were reviewed by community nurses to ascertain their information.

Assessment of ADL, Cognitive Function, Neurobehavioral Function, Mood and Serum Lipid Analysis

The questionnaire regarding the ADL was conducted in 1992 and 2001 in the same manner as was used in our previous study (*22*). Briefly, ADL were assessed with respect to the following seven items: walking, ascending and descending stairs, feeding, dressing, using the toilet, bathing, and grooming. Each ADL item was scored on a 0–3 scale: 0 = completely dependent, 1 = needs a lot of help, 2 = needs some help, and 3 = completely independent. The scores for these seven items were summarized to obtain a total ADL score ranging from 0 to 21. When a subject did not maintain a score of 21 or 20 points in 2001, he or she was defined as a person that was losing independence.

The mini-mental state examination (MMSE) was used to evaluate each subject's level of cognitive functioning (*23*). The Up and Go test was used to evaluate neurobehavioral function (*24*). This latter test measures, in s, the time it takes the subject to stand up from an armchair, walk a distance of 3 m, walk back to the chair, and sit down again. This simple test is a comprehensive evaluation of the subject's balance, gait speed, and functional ability. Since Okumiya and co-workers (*25*) reported its usefulness in predicting a decline in ADL in the Japanese community-dwelling elderly, the test has been widely accepted for this purpose in many fields. The Geriatric Depression Scale 15 (GDS 15) was also used to evaluate the mood of the subjects (depressive state) (*26*). Total serum cholesterol and serum high-density lipoprotein (HDL) cholesterol were analyzed in 1992.

During the period between 1992 and 2001, a total of 125 subjects (66 men, 59 women) died. In addition, the information regarding the events of stroke, myocardial infarction, congestive heart failure, and bone/joint diseases as causes of disability were collected by checking the responses provided on the annual questionnaire and the subjects' medical records.

Written informed consent was obtained from each subject at the time of the annual questionnaire. Our study was approved by the Research Ethics Committee of Kochi Medical School, Kochi University, Japan.

Statistical Analysis

All of the values were expressed as mean±SD. Mean values among the groups were compared using ANOVA. A χ^2 test was used to compare the 4 groups with respect to total mortality and incidence of stroke, as well as other CVDs. A logistic multivariate analysis was used to identify the factors that predicted a loss of functional independence or the survival and maintenance of functional independence 9 years after the initial assessment, using Stat View 5.0 for Windows (SAS Institute Inc., Cary, USA).

Table 2. Total/CVD Death and Non-Fatal Stroke

	NC (n=159)	NM (n=30)	HS (n=207)	HM (n=65)
Total death (%)*	36 (22.6)	3 (10.0)	62 (30.0)	24 (36.9)
Non-fatal stroke(%)	16 (10.1)	1 (3.3)	12 (5.8)	4 (6.2)
CVD death (%)	17 (10.7)	1 (3.3)	24 (11.6)	11 (16.9)
CVD events (%)	33 (20.8)	2 (6.7)	36 (17.4)	15 (23.1)

NC, normotensive/controlled; NM, normotensive/morning-dominant; HS, hypertensive/sustained; HM, hypertensive/morning-dominant; CVD, cardiovascular disease, including stroke. *ANOVA $p<0.1$.

Results

The distribution of mSBP and dSBP are shown in Fig. 1. The subjects were classified into the following 4 groups:

Hypertensive/morning-dominant (HM: mSBP≥135 mmHg, dSBP≥15 mmHg; n=65), hypertensive/sustained (HS: mSBP≥135 mmHg, dSBP<15 mmHg; n=207), normotensive/morning-dominant (NM: mSBP<135 mmHg, dSBP≥15 mmHg; n=30), and normotensive controlled (NC: mSBP<135 mmHg, dSBP<15 mmHg; n=159). The NC group, which was expected to be the lowest risk group because both the mSBP and the dSBP were lower than others, was used for reference.

A total of 461 elderly subjects, who were 75 years of age or older in 1992, were followed for 9 years until 2001 (Fig. 2). During that interval, 125 (27%) subjects died; 53 of these subjects had died of stroke and other CVDs. A total of 336 of the subjects were alive 9 years later (2001). One hundred-eighteen subjects had undergone a loss of their functional independence (HM, 17 [41%]; HS, 65 [45%]; NM, 7 [26%]; NC, 29 [24%]).

The basic characteristics of the 4 groups in 1992 are shown in Table 1. The subjects in the NC group were younger than those in the other 3 groups. The percentage of subjects who were taking antihypertensive agents was also the lowest in the NC group. There were no significant differences in terms of sex, PR, total serum cholesterol, HDL cholesterol, the scores of ADL, MMSE, the Up and Go test, or history of CVD among the 4 groups. There were also no differences in the scores on the GDS 15, history of bone/joint diseases, current and past cigarette smoking, and current intake of alcohol (data not shown).

Table 2 shows the total number of deaths, the number and percentage of deaths caused by stroke and other CVDs, and the incidence of non-fatal stroke during the 9-year follow-up period in the 4 groups. Although there was a difference in the total number of deaths among the 4 groups before adjustment for age, the significance of this difference disappeared after adjustment for age. There were no significant differences in the percentage of deaths from stroke or other CVDs. Although 33 subjects suffered from symptomatic strokes, no significant differences were seen in the incidence of strokes among the 4 groups.

The risk factors for loss of functional independence are shown in Table 3. Although a non-fatal event of stroke was one of the most important risk factors for loss of functional independence, HM and HS were also important risk factors, even after adjustment for age, sex, antihypertensive therapy, scores on the Up and Go test in 1992, and the ADL scores in 1992. The adjusted odds ratio (OR) of the HM group (12.2) was significantly higher than that of the HS group (3.78). Therefore, values of mSBP≥135 mmHg and dSBP≥15 mmHg were independent risk factors for a loss of functional independence (Fig. 3).

The factors associated with successful aging that contributed to the survival and maintenance of functional independence, even among the most elderly (age of 84 or older), are shown in Table 4. Although the non-fatal event of stroke was a significantly negative determinant, the HM and HS also remained as significant independent negative determinants of successful aging, after adjustment for age, sex, antihypertensive therapy, scores on the Up and Go test in 1992, and ADL scores in 1992.

As regards the elderly people aged 75 years or older living in the community, values of mSBP≥135 mmHg and dSBP≥15 mmHg were independent determinants of a loss of functional independence or successful aging, even when non-fatal stroke and these home SBP variables were simultaneously incorporated into a logistic multivariate analysis model.

In addition, since many of our subjects with morning hypertension had high home SBP, we added dSBP (≥15 mmHg) to the same model of multivariate logistic analysis, in order to elucidate whether dSBP was an independent determinant of a loss of functional independence or alive and independence. dSBP remained a significant determinant of a loss of independence (adjusted OR: 3.84, 95% confidence interval [CI]: 1.003–14.73), or alive and independence (adjusted OR: 0.46, 95% CI: 0.183–0.973), in our hypertensive subjects.

Discussion

Our prospective longitudinal study evaluating the maintenance of independence in the elderly aged 75 years or older demonstrated that a mean home SBP of ≥135 mmHg was a significantly important risk factor for a loss of functional independence. In addition, morning hypertension was an

Table 3. Independent Risk Factors for Loss of Independence in 336 Survivors

Factors	Adjusted odds ratio	95% CI	*p*
Stroke	17.4	3.67–82.8	0.0003
HM	12.2	3.00–50.0	0.0005
HS	3.78	1.45–9.83	0.0064
Age	1.17	1.05–1.30	0.0036

Data were adjusted for sex, antihypertensive therapy, Up and Go score, and activities of daily living (ADL) score in 1992. CI, confidence interval; HM, hypertensive/morning-dominant; HS, hypertensive/sustained.

Table 4. Independent Negative Factors for Survival and Maintenance of Independence (n=461)

Factors	Adjusted odds ratio	95% CI	*p*
Stroke	0.058	0.012–0.273	0.0003
HM	0.082	0.020–0.334	0.0005
HS	0.271	0.104–0.704	0.0073
Age	0.855	0.768–0.951	0.0038

Data were adjusted for sex, antihypertensive therapy, Up and Go score, and activities of daily living (ADL) score in 1992. CI, confidence interval; HM, hypertensive/morning-dominant; HS, hypertensive/sustained.

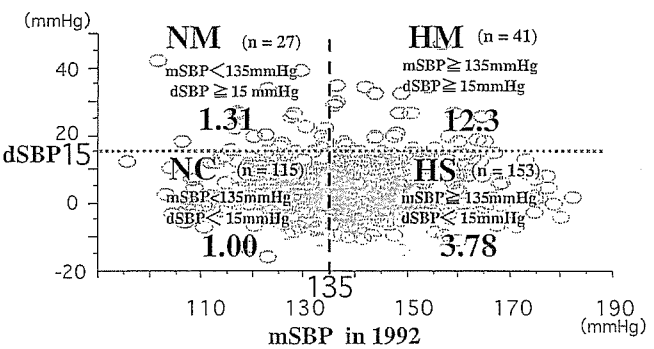

Fig. 3. *Adjusted odds ratios for loss of independence among the 4 groups. The abbreviations are the same as those introduced in Fig. 1.*

important independent predictor for the functional prognosis of our elderly subjects. The significance of dSBP should be further evaluated.

There were no differences in mortality and incidence of non-fatal stroke among the 4 groups. However, when a loss of functional independence was selected as the endpoint, significant differences were found among these groups. Home BP monitoring in the morning and in the evening was useful in predicting functional prognosis in elderly subjects aged 75 years or older.

Recent large clinical trials have clarified the importance of BP control, even among the elderly (*7–9*). However, the optimum home BP value for the elderly has not been established, and further prospective studies on the elderly will be necessary to define an adequate home BP value (*27*).

In the present study, there was no significant difference in the incidence of CVD death, stroke, and other CVD events among the 4 groups. Although the reason for this result is uncertain, further studies with a larger number of subjects may resolve this ambiguity.

Since a relationship between elevation of BP in the morning and stroke and other CVD events (*14–17*) has been reported, the importance of morning BP has been emphasized in studies of home BP monitoring (*28, 29*). However, in most of these studies the mortality and morbidity of stroke and other CVDs, as well as organ damage, were selected as the endpoints. Functional independence, which is important for the elderly as well as for the social economy, is not mentioned in these previous studies. Thus, in our present study, we added a loss of functional independence and successful aging as two new endpoints for geriatric study. Furthermore, we evaluated morning–evening home BP differences in terms of the usefulness of this information for the prognosis of the elderly aged 75 years or older.

Skoog *et al.* (*30*) reported the relationship between the presence of hypertension at the age of 70 and the development of dementia 10 to 15 years later. In subsequent large studies including SCOPE (*10*), the association between impaired cognitive function and BP values has been evaluated, although sufficient data on the relationship between BP control and cognitive function have yet to be accumulated. In our previous study (*31*), a J-curve phenomenon was demonstrated with respect to the profile of the association between BP values and cognitive function 3 years later in an elderly sample. Those findings indicate that BP exerted an effect on cognitive function, not only in the group with high BP, but also in the group with low BP. In our previous study, casual BP was measured twice with the subject in the supine position at the time of physical examination. Here, to avoid the inclusion of various other factors affecting BP measurements, we used 20 home BP measurements in order to calculate the mean value. This method of measurement appeared to have eliminated some of the potential problems with BP monitoring.

Because the follow-up period was so long (9 years), it was difficult to reexamine cognitive function in all of the subjects examined in 2001; some subjects were too old for us to obtain reliable data from them (*i.e.*, among those at least aged 84 years of age and older). Due to our small sample size in the MMSE evaluation (n=64, 19%), we did not observe any significant differences between the group with high home BP values (≥135 mmHg) and the group with normal home BP values (<135 mmHg). There were also no significant differences in dSBP (≥15 mmHg). Evaluation of the cognitive functions (MMSE) of the most elderly subjects included in the sample was difficult; thus, an appropriate, reliable method

will still need to be developed for the evaluation of this group in future studies.

A variety of factors, including stroke events and other CVDs, as well as the progression of bone/joint diseases and dementia, contributes to disability among the elderly (*32*). The present study demonstrated for the first time that those elderly persons with a mean home SBP≥135 mmHg were susceptible to a loss of functional independence, even if they did not experience an event of symptomatic stroke. However, the present study did not reveal any direct mechanism to generate this relationship between hypertension reflected by the home BP monitoring value and a loss of independence. The relationships between hypertension or morning BP elevation and pathological conditions such as asymptomatic small infarctions and white matter lesions have previously been reported (*33–36*). It is thus possible that these lesions are related to BP elevation and may be involved in the impairment of functional abilities required for daily life. To clarify the association between home BP values, asymptomatic brain lesions, and disability among the very elderly, further study is warranted.

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ORIGINAL ARTICLE

Quantitative analysis of carotid atherosclerotic lesions and high-sensitivity C-reactive protein in community-dwelling elderly 80 years or older

Ichiro Miyano,[1] Jun Takata,[1] Masanori Nishinaga,[1] Kiyohito Okumiya,[2] Tomio Hamada,[1] Toru Kubo,[1] Yukari Morita,[1] Makoto Okawa,[1] Naohito Yamasaki,[1] Kyoko Sato,[1] Kozo Matsubayashi[3] and Yoshinori Doi[1]

[1]*Department of Medicine and Geriatrics, Kochi Medical School, Kochi,* [2]*Research Institute for Humanity and Nature, and* [3]*Center for South-East Asian Studies, Kyoto University, Kyoto, Japan*

Aim: To investigate the association between the carotid atherosclerotic lesions assessed by high-resolution ultrasonography and high-sensitivity C-reactive protein (hs-CRP) in the community-dwelling elderly aged 80 years or older.

Methods: One hundred and seventy-nine community-dwelling elderly aged 65 years or older (78 ± 6 years, 69 men and 113 women) participated in this study. High-resolution B-mode ultrasonography was performed on the common carotid arteries. Intima-media thickness (IMT) was measured using automatic measuring system and compared with standardized examinations included blood pressure, body mass index, hemoglobin-A1c, cholesterol, creatinine, uric acid, fibrinogen and hs-CRP.

Results: Subjects were divided into two age groups: young-old aged 65–79 years (113 subjects, 74 ± 3 years) and old-old aged 80 years or older (66 subjects, 84 ± 3 years). The maximum (max) IMT was significantly increased in the old-old compared to that of the young-old (1.7 ± 1.0 *vs* 1.4 ± 0.6 mm; $P = 0.02$). Multivariate analysis showed that hs-CRP was the strongest predictor of thickened max IMT in the young-old ($P = 0.022$). However, it was not the predictor of thickened max IMT in the old-old.

Conclusions: Depending on age, hs-CRP may have different meanings in the atherosclerotic process. In particular, the predictive power of hs-CRP as a marker of atherosclerotic process was less significant in subjects aged 80 years or older.

Keywords: automatic measuring system, carotid atherosclerotic lesions, community-dwelling elderly, high-sensitivity C-reactive protein (hs-CRP), intima-media thickness (IMT).

Introduction

The progression of atherosclerosis has come to be recognized as a process of chronic inflammatory responses.[1–4] Many circulating markers such as high-sensitivity C-reactive protein (hs-CRP) and cytokines have been reported to be potential predictors for the presence of cardiovascular disease and the occurrence of future cardiovascular events in subjects from middle

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Correspondence: Dr Yoshinori Doi, MD, Department of Medicine and Geriatrics, Kochi Medical School, Oko-cho, Nankoku-shi, Kochi 783-8505, Japan. Email: ydoi@med.kochi-u.ac.jp

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age to old age up to 79, but not in the elderly population over 80 years old.[5–9]

Recently, carotid ultrasonography has been used to estimate carotid atherosclerosis. The indices of severity such as plaque number, plaque score and the maximum intima-media thickness (max IMT) were related to age, systolic blood pressure, serum cholesterol, blood sugar level and smoking. These indices are also associated with cardiovascular events such as myocardial infarction and stroke.[10–13]

In this study, we quantitatively examined the carotid atherosclerotic lesions using high-resolution ultrasonography and their association with hs-CRP and conventional risk factors in the community-dwelling elderly in order to investigate the significance of these factors in the elderly aged 80 years or older.

Methods

Study population

Between July 2003 and August 2004, we performed cardiovascular health checks in the town of Kahoku (population: approximately 6000, 38% of them aged 65 years or older). One hundred and eighty-two community-dwelling elderly aged 65 years or older (mean: 78 ± 6 years, 69 men and 113 women) participated in this study with informed consent. Standardized examinations included casual systolic and diastolic blood pressures in a sitting position, body mass index (BMI), hemoglobin-A1c (Hb-A1c), cholesterol (total, low-density lipoprotein [LDL], and high-density lipoprotein [HDL] cholesterol), creatinine, uric acid, fibrinogen and hs-CRP. Participants answered questionnaires including smoking and history of hypertension, hyperlipidemia and diabetes mellitus.

Subjects who had uncontrolled cardiovascular diseases and were thought to have acute inflammatory disease, autoimmune disease and cancer were not included. Three subjects with hs-CRP values exceeding 1.0 mg/dL were also excluded from the study because the American Heart Association (AHA) and Centers for Disease Control and Prevention (CDC) scientific statement concerning these markers of inflammation stated that hs-CRP values exceeding 1.0 mg/dL should be discarded; therefore, further examination for a non-cardiovascular source of inflammation was necessary.[14] A total of 179 subjects (mean age; 78 ± 6 years; 69 men and 110 women) were analyzed.

Carotid ultrasonography

High-resolution B-mode carotid ultrasonography was performed using an 11-MHz probe (Toshiba Nemio; Toshiba Medical Systems, Tokyo, Japan) on both sides of the common carotid arteries with subjects in the supine position. All ultrasound studies were carried out by the same experienced physician, blinded to the clinical information of the subjects. Bilateral common carotid arteries were scanned in the axial view from the proximal portion to the bifurcation, followed by scanning in the longitudinal view. Digital images of carotid ultrasonography were stored in a computer for the quantitative measurement of IMT. Maximum IMT was derived from the 60 consecutive measured points in 2-cm segment at the far wall, just proximal to the bulb of the common carotid artery, using an automatic Intima Scope measuring system (Media Cross, Tokyo, Japan; Fig. 1). The basic principle of image processing methods adopted in this system was previously described. The results of the automatic analyzing system showed significant relation with manual system and less inter-observer variability than manual analysis.[15–18] When morphologically protruded plaques were observed in this segment, max IMT was measured including the plaques.[19,20]

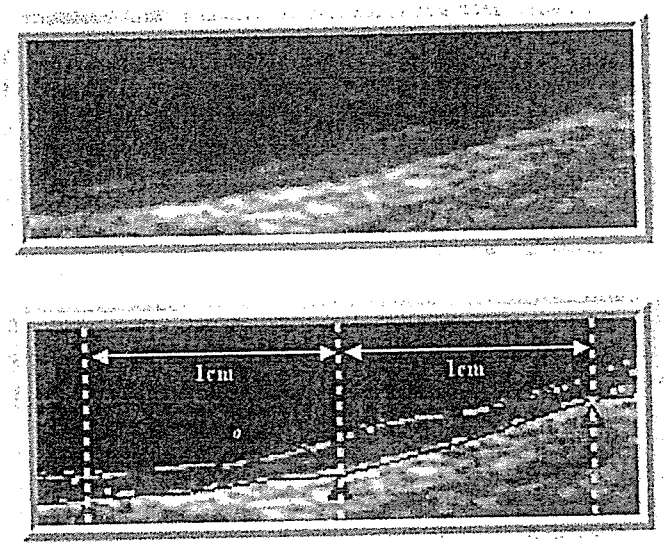

Figure 1 Digital image of ultrasonography of common carotid artery (top). Edge points of intima and adventitia are traced using the change of echo intensity (bottom). Maximum intima-media thickness (IMT) was derived from the 60 consecutive measured points in the 2-cm segment of the far wall, using an automatic measuring system of Intima Scope (Media Cross).

Measurement of hs-CRP

Blood samples were collected in tubes containing citric acid and stored at −80°C. A latex phelometer was used for the measurement of hs-CRP with a sensitivity of 0.004 mg/dL (N-latex CRP II, Dade Behring, Tokyo, Japan).

Statistical analysis

Mean values were compared using ANOVA and categorical variables were compared using the χ^2 test. A logistic

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multivariate analysis was used to identify the predictive factors for thickened max IMT. All statistical analyses were performed with Stat View, version 5.0 for Windows (SAS Institute, Cary, NC, USA).

Results

Baseline characteristics

Baseline characteristics of the subjects are shown in Table 1. The subjects were divided into two age groups: young-old aged 65–79 years (113 subjects; mean: 74 ± 3 years) and old-old aged 80 years or older (66 subjects, mean; 84 ± 3 years) for comparison.

The two age groups were comparable for male-to-female ratio, history of hypertension, hyperlipidemia, and past and current smoking. Casual blood pressure levels at the time of examination were similar in both groups. BMI was significantly higher in the young-old than in the old-old ($P = 0.023$). Serum Hb-A1c was significantly higher ($P = 0.026$) and history of diabetes tended to be higher ($P = 0.061$) in the young-old than in the old-old. On the other hand, serum creatinine was significantly higher in the old-old ($P = 0.003$). There was no significant difference in hs-CRP between the two groups.

Quantitative carotid ultrasonography

The value of max IMT of the common carotid artery was significantly increased in the old-old ($P = 0.016$). Moderate sclerotic lesions with a max IMT of >2.3 mm (mean + 1 SD of all 179 subjects) were more frequently found in the old-old group ($P = 0.024$). Because a value of max IMT >1.1 mm is generally considered as normal,[21] two age groups were evaluated according to the value of max IMT: (i) normal IMT (<1.1 mm); (ii) mildly thickened IMT (1.1–2.2 mm); and (iii) moderately

Table 1 Basic characteristics of all subjects and two age groups

	All	Young-old (65–79 years)	Old-old (≥80 years)	*P* (Young-old *vs* old-old)
n	179	113	66	
Men/Women	69/110	43/70	26/40	0.859
Age (years)	78 ± 6	74 ± 3	84 ± 3	<0.001
BMI (kg/m^2)	22.5 ± 3.5	23.0 ± 3.2	21.8 ± 3.7	0.023
SBP (mmHg)	143.4 ± 21.6	144.8 ± 21.2	141.0 ± 22.2	0.026
DBP (mmHg)	80.6 ± 11.9	81.1 ± 11.4	79.7 ± 12.7	0.479
Hypertension (%)	85 (47.5)	55 (48.7)	30 (45.5)	0.677
Diabetes (%)	18 (10.1)	15 (13.3)	3 (4.5)	0.061
Hyperlipidemia (%)	26 (14.5)	18 (15.9)	8 (12.1)	0.497
Smoking				
No Smoking (%)	132 (73.7)	85 (75.2)	47 (71.2)	0.599
Past Smoking (%)	32 (17.9)	18 (15.9)	14 (21.2)	0.421
Current Smoking (%)	15 (8.4)	10 (8.9)	5 (7.6)	0.999
Hb-A1c (%)	5.3 ± 0.7	5.4 ± 0.7	5.2 ± 0.5	0.026
T-chol (mg/dL)	192.4 ± 33.6	195.9 ± 33.7	186.5 ± 32.9	0.069
LDL-chol (mg/dL)	114.4 ± 27.8	116.4 ± 27.4	110.9 ± 28.2	0.199
HDL-chol (mg/dL)	55.2 ± 13.8	55.4 ± 14.2	54.7 ± 13.4	0.764
Creatinine (mg/dL)	0.78 ± 0.17	0.75 ± 0.16	0.83 ± 0.18	0.004
Uric acid (mg/dL)	5.4 ± 1.3	5.4 ± 1.3	5.3 ± 1.2	0.602
Fibrinogen (mg/dL)	335.8 ± 77.5	334.0 ± 81.2	338.8 ± 71.1	0.689
hs-CRP (mg/dL)	0.12 ± 0.17	0.12 ± 0.18	0.12 ± 0.17	0.950
max IMT (mm)	1.53 ± 0.77	1.43 ± 0.62	1.71 ± 0.96	0.016
<1.1 mm (%)	56 (31.3)	38 (33.6)	18 (27.3)	0.408
1.1–2.2 mm (%)	99 (55.3)	65 (57.5)	34 (51.5)	0.441
>2.3 mm (%)	24 (13.4)	10 (8.9)	14 (21.2)	0.024

BMI, body mass index; DBP, diastolic blood pressure; Hb-A1c, hemoglobin-A1c; HDL-chol, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; IMT, intima-media thickness; LDL-chol, low-density lipoprotein cholesterol; SBP, systolic blood pressure; T-chol, total cholesterol.

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Table 2 Clinical and laboratory findings in each age group with three max IMT levels

Max IMT	Young-old (65–79 years old [$n = 113$])			Old-old (≥80 years old [$n = 66$])		
	<1.1	1.1–2.2	>2.3	<1.1	1.1–2.2	>2.3
	$n = 38$	$n = 65$	$n = 10$	$n = 18$	$n = 34$	$n = 14$
Men/Women	12/26	26/39	5/5	6/12	15/19	5/9
BMI (kg/m^2)	22.6 ± 3.0	23.4 ± 3.4	21.9 ± 2.3	21.5 ± 3.1	21.9 ± 4.3	21.7 ± 2.8
SBP (mmHg)	145.2 ± 20.6	144.5 ± 22.4	145.5 ± 16.6	136.8 ± 18.4	144.4 ± 25.4	138.4 ± 17.6
DBP (mmHg)	81.7 ± 12.2	80.9 ± 11.4	80.0 ± 9.5	75.9 ± 10.9	83.3 ± 14.4	75.9 ± 7.2
Hypertention (%)	14 (36.8)	36 (55.4)	5 (50)	9 (50)	14 (41.2)	7 (50)
Diabetes (%)	5 (13.2)	10 (15.4)	0 (0)	0 (0)	2 (5.9)	1 (7.1)
Hyperlipidemia (%)	5 (13.2)	10 (15.4)	3 (30)	5 (27.8)	2 (5.9)	1 (7.1)
Smoking (%)						
No Smoking (%)	32 (84.2)	48 (73.8)	5 (50)	12 (66.7)	23 (67.6)	12 (85.7)
Past Smoking (%)	5 (13.2)	10 (15.4)	3 (30)	5 (27.8)	7 (20.6)	2 (14.3)
Current Smoking (%)	1 (2.6)	7 (10.8)	2 (20)	1 (5.6)	4 (11.8)	0 (0)
Hb-A1c (%)	5.2 ± 0.5	5.5 ± 0.9	5.4 ± 0.5	4.8 ± 0.6	5.2 ± 0.5***	5.3 ± 0.5***
T-chol (mg/dL)	194.7 ± 33.2	199.0 ± 34.6	180.7 ± 27.0	182.7 ± 36.1	189.8 ± 33.9	183.1 ± 27.1
LDL-chol (mg/dL)	116.9 ± 25.1	117.7 ± 29.0	106.4 ± 25.9	108.2 ± 31.2	113.9 ± 28.8	107.1 ± 23.5
HDL-chol (mg/dL)	55.0 ± 13.6	55.8 ± 14.1	54.1 ± 17.5	56.8 ± 12.4	54.1 ± 14.7	53.6 ± 11.8
Creatinine (mg/dL)	0.74 ± 0.18	0.74 ± 0.16	0.81 ± 0.15	0.81 ± 0.12	0.83 ± 0.20	0.84 ± 0.20
Uric acid (mg/dL)	5.1 ± 1.0	5.5 ± 1.4	6.0 ± 1.4*	5.3 ± 1.3	5.3 ± 1.3	5.4 ± 1.1
Fibrinogen (mg/dL)	323.5 ± 77.8	336.0 ± 81.0	361.0 ± 96.0	321.2 ± 64.8	349.7 ± 64.0	334.9 ± 92.8
hs-CRP (mg/dL)	0.09 ± 0.17	0.12 ± 0.16	0.24 ± 0.26**	0.07 ± 0.10	0.14 ± 0.18	0.15 ± 0.18

*$P < 0.05$ compared with group of max IMT <1.1 mm; **$P < 0.05$ compared with other two groups; ***$P < 0.01$ compared with group of max IMT < 1.1 mm.

thickened IMT (>2.3 mm). The comparison of clinical and laboratory findings in each age group with three max IMT levels are shown in Table 2.

In the young-old group, hs-CRP was significantly higher in those with moderately thickened max IMT than others ($P < 0.05$). Serum uric acid was significantly higher in those with moderately thickened max IMT than those with normal IMT ($P = 0.039$). There were no significant differences in other conventional risk factors.

In the old-old group, hs-CRP did not show significant differences in three max IMT subgroups. Serum Hb-A1c levels were significantly higher in those with moderately and mildly thickened max IMT than those with normal IMT ($P < 0.01$).

High-sensitivity C-reactive protein and max IMT

The relationship between hs-CRP and max IMT in the two age groups is shown in Figure 2. In the old-old group, no significant relationship was found between hs-CRP and max IMT, although it was present in the young-old group.

Age, sex and conventional risk factors such as diabetes (including elevated Hb-A1c more than 5.8% at health check), hypertension, hyperlipidemia and BMI were entered into multivariate analysis with hs-CRP for prediction of moderately thickened IMT. A logistic multivariate analysis showed that hs-CRP was not the predictor of moderately thickened IMT in the old-old

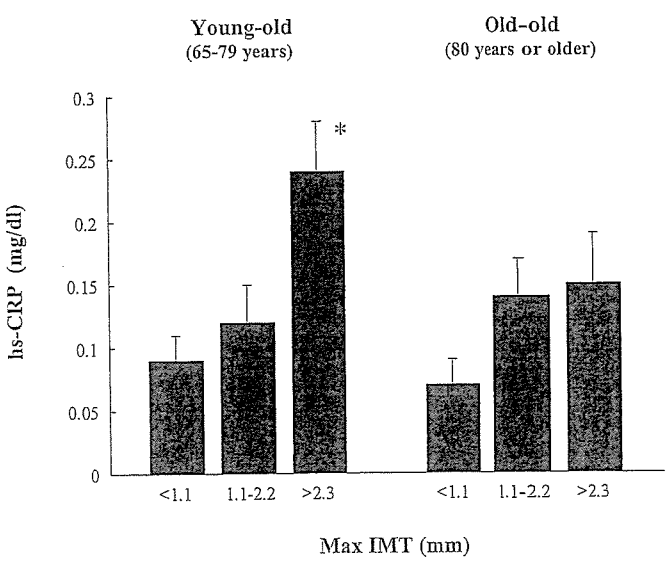

Figure 2 High-sensitivity C-reactive protein (hs-CRP) and max IMT in each age group. *$P < 0.05$ compared with other two groups.

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Table 3 Adjusted odds ratios of the moderately thickened IMT and selected factors

Risk factors	Adjusted odds ratio	95% CI	*P*
Young-old (65–79 years)			
Age (years)	1.12	0.86–1.46	0.415
Female	0.45	0.10–1.98	0.293
BMI (kg/m^2)	0.89	0.70–1.14	0.344
Hypertension	1.15	0.22–5.98	0.866
Diabetes	1.51	0.31–7.37	0.612
Hyperlipidemia	5.07	0.89–28.79	0.067
hs-CRP (mg/dL)	31.52	1.65–600.79	0.022
Old-old (80 years or older)			
Age (years)	0.92	0.73–1.17	0.487
Female	1.16	0.31–4.32	0.824
BMI (kg/m^2)	0.93	0.77–1.12	0.424
Hypertension	1.76	0.43–7.27	0.433
Diabetes	5.82	1.02–33.08	0.047
Hyperlipidemia	0.38	0.04–3.94	0.418
hs-CRP (mg/dL)	1.42	0.03–60.08	0.855

95% CI, 95% confidence interval.

group, although hs-CRP was the strongest predictor in the young-old group ($P = 0.022$).

Considering the skewed distribution of hs-CRP, ANOVA and multivariate analysis using natural-log-transformed data were also performed. In the young-old group, both analyses showed consistent results. In the old-old group, univariate analysis showed that hs-CRP in normal IMT subgroup was lower than the other two groups ($P < 0.05$). However, multivariate analysis did not demonstrate the predictive power of hs-CRP for moderately thickened IMT in the old-old group.

Diabetes was a significant predictor for increased max IMT only in the old-old-group ($P = 0.047$). Hyperlipidemia tended to have a relation to thickened max IMT only in young-old but was statistically insignificant (Table 3).

Discussion

In the present study, using high-resolution ultrasonography with a quantitative measurement system of vascular wall thickness, we have demonstrated that there was no relationship between hs-CRP and max IMT in the subjects aged 80 years or older, although the significant relationship was present in those aged 65–79 years. Although the progression of atherosclerosis has been recognized as a process of chronic inflammation, it is possible that depending on age, hs-CRP may have different meaning on atherosclerotic process.

Maximum intima-media thickness and hs-CRP

Inflammatory processes play an important role in many stages of atheroma formation from leukocyte recruitment to eventual plaque rupture. High levels of markers of the inflammatory cascade, such as P-selectin,[22] interleukin-6,[23,24] tumor necrosis factor-α[25] and CRP have proved to be strong predictors of cardiovascular events. Of all these markers, CRP has been the most extensively used in clinical investigations.[26–28] In particular, hs-CRP can be a better marker for atherosclerotic lesions in the earlier stages compared with the conventional risk factors.[29,30] Although CRP has also been associated with cardiovascular events and mortality in healthy individuals in their 60s and 70s,[5–9] there are few studies that have addressed the elderly over 80 years of age.[31–33]

Because carotid atherosclerosis is a good indicator of general atherosclerosis, and therefore related to cardiovascular disease and mortality, carotid ultrasonography has recently been employed to estimate the severity and progression of atherosclerotic lesions. However, conventional measurement of max IMT has presented difficulties in accuracy,[27] because the determination of the site of maximum wall thickness is dependent on visual judgment and the number of points of measurement are insufficient. To solve this problem, in the present study, high-resolution B-mode ultrasonography of the common carotid artery was performed with an 11-MHz probe and all digital images were stored in a computer datafile. Using an automatic measuring system of vascular wall thickness, the IMT was measured at 60 consecutive points in a 2-cm wide segment and then the greatest IMT value was defined as the max IMT.

In the present study, a relationship of max IMT and hs-CRP and the conventional risk factors was evaluated in the community-dwelling elderly aged 65 years or older, particularly focusing on those aged 80 years or older. Our results showed that the max IMT of the

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