19 Shimamoto K, Ando K, Fujita T, Hasebe N, Higaki J, Horiuchi M *et al.* The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2014). *Hypertens Res* 2014; **37**: 253–387.
20 Tsutsui T, Muramatsu N. Care-needs certification in the long-term care insurance system of Japan. *J Am Geriatr Soc* 2005; **53**: 522–527.
21 Tsutsui T, Muramatsu N. Japan's universal long-term care system reform of 2005: costs and realizing a vision. *J Am Geriatr Soc* 2007; **55**: 1458–1463.
22 Ogihara T, Matsuoka H, Rakugi H. Practitioner's trial on the efficacy of antihypertensive treatment in elderly patients with hypertension II (PATE-hypertension II study) Japan. *Geriatr Gerontol Int* 2011; **11**: 414–421.
23 Cox DR. Regression models and life tables. *J R Stat Soc Series B Stat Methodol* 1972; **34**: 187–220.
24 Concato J, Feinstein AR, Holford TR. The risk of determining risk with multivariable models. *Ann Intern Med* 1993; **118**: 201–210.
25 Puri KS, Suresh KR, Gogtay NJ, Thatte UM. Declaration of Helsinki, 2008: implications for stakeholders in research. *J Postgrad Med* 2009; **55**: 131–134.
26 Iritani O, Koizumi Y, Hamazaki Y, Yano H, Morita T, Himeno T *et al.* Association between blood pressure and disability-free survival among community-dwelling elderly patients receiving antihypertensive treatment. *Hypertens Res* 2014; **37**: 772–778.
27 Kannel WB. Prevalence and implications of uncontrolled systolic hypertension. *Drugs Aging* 2003; **20**: 277–286.
28 Greenberg JD, Tiwari A, Rajan M, Miller D, Natarajan S, Pogach L. Determinants of sustained uncontrolled blood pressure in a national cohort of persons with diabetes. *Am J Hypertens* 2006; **19**: 161–169.
29 Wen CY, Chen Y, Tang HL, Yan CH, Lu WW, Chiu KY. Bone loss at subchondral plate in knee osteoarthritis patients with hypertension and type 2 diabetes mellitus. *Osteoarthr Cartilage* 2013; **21**: 1716–1723.
30 Birkenhäger WH, Forette F, Staessen JA. Dementia and antihypertensive treatment. *Curr Opin Nephrol Hypertens* 2004; **13**: 225–230.

J Exp Clin Med 2014;6(2):64–65

Contents lists available at ScienceDirect

Journal of Experimental and Clinical Medicine

journal homepage: http://www.jecm-online.com

LETTER TO THE EDITOR

A Growing Mass in the Mediastinum: Hiatus Hernia

Bowditch first published a description of a hiatus hernia (HH) in 1853. In 1919, Soresi was the first to surgically reduce a HH. During the first half of the 20th century, the association between gastroesophageal reflux disease (GERD) and HH was established. HHs are classified into four types: type I indicates sliding hernia; type II, paraesophageal hernia (incidence ≤5%); type III, mixed sliding and paraesophageal hernia; and type IV, herniation of additional organs (colon, omentum, and spleen).[1] A giant HH is a hernia that includes at least 30% of the stomach in the thorax, and most commonly is a type III hernia.[2] There are two potential mechanisms of giant HHs: (1) GERD leads to esophageal scarring and shortening with traction on the gastroesophageal junction and gastric herniation; and (2) chronic positive pressure on the diaphragmatic hiatus with a propensity to herniation leads to gastric displacement into the thorax, resulting in causing GERD.[2] We report an elderly patient with a growing mass in the mediastinum on the roentgenogram, who was already treated for erosive esophagitis.

An 85-year-old female patient presented himself with a large mass in mediastinum on the chest roentgenogram. The patient had already received both treatments with a proton pump inhibitor for erosive esophagitis and a calcium channel blocker for hypertension. She had neither chest oppression nor respiratory distress. Her physical examination results showed that she was neither anemic nor febrile. Her blood pressure indicated 125/70 mmHg on the supine position. In fact, her chest roentgenography revealed a large mass overlapping with the heart (Figure 1A, arrows), which included the air–fluid level (arrowheads), with a pulmonary scar in the right lower field. Retrospective analyses using the chest roentgenograms showed that the mass was found on the film obtained 2 years ago (Figure 1B, arrows), and that it was not detected on the film 4 years ago (Figure 1C). Chest computed tomography indicated a large HH with intrathoracic stomach located behind the left atrium (Figure 1D) as previously described.[3] A diagnosis of HH type III was made. At follow-up 1 year later, the patient was asymptomatic, although she received no further treatment.

Lim et al[4] have recently reported a unique case of a massive HH in a 93-year-old woman patient, compressing on the left atrium, mimicking a left atrial mass. A massive HH and the thoracic stomach were also illustrated by barium swallow as images in cardiovascular medicine during left atrial catheter ablation for atrial fibrillation.[5] Echocardiography is an investigational tool for identifying cardiac masses. However, detection of extracardiac masses using echocardiography may lead to a misdiagnosis. The result from another asymptomatic patient with a paracardiac mass in the right lower lobe suggests the remarkable accuracy of chest computed tomography for diagnosing a massive HH containing the whole stomach and fatty omental tissue.[3] A case of massive HH masquerading as a tension pneumothorax was also reported.[6] Clinicians should consider a large HH when examining patients with a mass that is located behind the heart in the mediastinum on the roentgenogram. Our images concerning HH appear to be instructive for clinicians.

References

1. Landreneau RJ, Del Pino M, Santos R. Management of paraesophageal hernias. *Surg Clin North Am* 2005;**85**:411–32.
2. Mittek MO, Andrade RS. Giant hiatal hernia. *Ann Thorac Surg* 2010;**89**:S2168–73.
3. Foresti V, Villa A, Tagliaferri B. Sliding massive hiatal hernia: diagnosis using computerized axial tomography. *Minerva Med* 1987;**78**:171–4.
4. Lim HS, Leong DP, Alasady M. Massive hiatus hernia mimicking a left atrial mass. *Heart Lung Circ* 2013;**22**:875–6.
5. Good E, Wells D, Cronin P, Morady F, Oral H. Images in cardiovascular medicine. Massive hiatal hernia and thoracic stomach illustrated by barium swallow during left atrial catheter ablation for atrial fibrillation. *Circulation* 2008;**118**:2011–2.
6. Chong CF, Lin YM, Chao CC, Shen ST, Huang TY. Massive hiatal hernia masquerading as a tension pneumothorax. *Am J Emerg Med* 2007;**25**:226–8.

Takashi Takahashi*
Laboratory of Infectious Diseases, Graduate School of Infection Control Sciences, Kitasato University, Tokyo, Japan

Masashi Okuro, Kunimitsu Iwai, Shigeto Morimoto
Department of Geriatric Medicine, Kanazawa Medical University, Ishikawa, Japan

* Corresponding author. Takashi Takahashi, 5-9-1, Shirokane, Minato-Ku, Tokyo 109-8641, Japan.
E-mail: T. Takahashi <taka2si@lisci.kitasato-u.ac.jp>.

Nov 6, 2013
Available online 17 March 2014

Conflicts of interest: The authors have no conflicts of interest to declare in relation to this article.

http://dx.doi.org/10.1016/j.jecm.2014.02.002

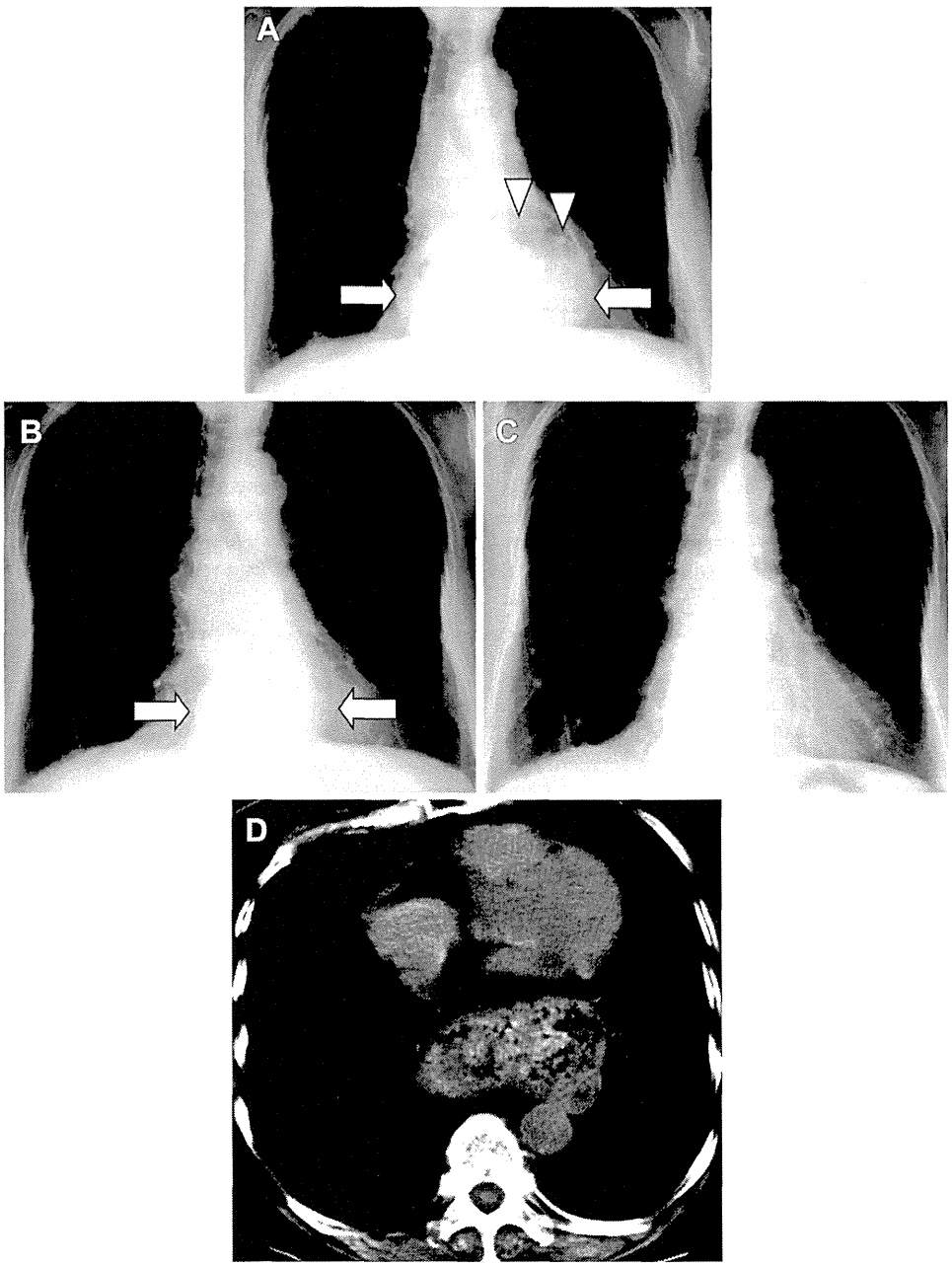

Figure 1 Chest roentgenography reveals (A) a large mass overlapping with the heart (arrows), which includes the air–fluid level (arrowheads), with a pulmonary scar in the right lower field. Retrospective analyses using the chest roentgenograms show that (B) the mass was found on the film obtained 2 years previously (arrows), and that (C) it was not detected on the film 4 years ago. (D) Chest computed tomography indicates a large hiatus hernia with intrathoracic stomach located behind the left atrium.

Hypertension Research (2014) 37, 772–778

www.nature.com/hr

ORIGINAL ARTICLE

Association between blood pressure and disability-free survival among community-dwelling elderly patients receiving antihypertensive treatment

Osamu Iritani[1], Yumi Koizumi[2], Yuko Hamazaki[2], Hiroshi Yano[1], Takuro Morita[1], Taroh Himeno[1], Tazuo Okuno[1], Masashi Okuro[1], Kunimitsu Iwai[1] and Shigeto Morimoto[1]

A reduction of elevated blood pressure (BP) is an important treatment goal in elderly hypertensive patients. However, excessive reduction of systolic BP (SBP) and/or diastolic BP (DBP) might be harmful in such patients. We investigated whether this was the case with regard to risk of incident disability or death in community-dwelling elderly subjects. We analyzed 570 patients receiving antihypertensive treatment aged 65–94 years. The endpoint was the composite outcome of incident disability, defined as first certification of a support/care need or death. Relationships among each of the four classes of SBP or DBP and the risk of incident disability or death were estimated using the Cox proportional hazards model. Over four years, 77 (13.5%) incident disabilities or deaths occurred. After adjustment for age, sex and variables selected according to their univariate analysis *P*-value <0.20, the risk of events was significantly higher in subjects with baseline SBP <120 mm Hg (hazard ratio (HR) $=2.81$, $P=0.023$) and $\geqslant 160$ mm Hg (HR $=4.32$, $P<0.001$), compared with subjects with baseline SBP of 140–159 mm Hg, who showed the lowest incidence of events. This J-curve relationship was observed in very elderly patients ($\geqslant 75$ years) but not in younger patients. Patients with SBP <120 mm Hg tended to have a higher risk of incident disability caused by cerebral events, and those with SBP $\geqslant 160$ mm Hg had a higher risk of incident disability caused by falls/bone fractures. These observations indicate that excessive BP reduction could cause discontinuance of disability-free survival in community-dwelling elderly patients.
Hypertension Research (2014) **37**, 772–778; doi:10.1038/hr.2014.67; published online 27 March 2014

Keywords: disability; elderly; J-curve; treatment

INTRODUCTION

Providing high-quality treatment to older adults with elevated blood pressure (BP), which is aimed at both the prevention of cardiovascular/cerebrovascular (CV) morbidity/mortality and the promotion of cognitive/physical function, is growing in importance because of the improved survival of patients with hypertension into old age. Many large-scale intervention trials, including a meta-analysis of eight large-scale intervention trials in elderly hypertensive patients aged $\geqslant 60$ years,[1] recent clinical trials limited to elderly patients aged $\geqslant 60$ years,[2–7] and Hypertension in the Very Elderly Trial,[8] which enrolled those aged $\geqslant 80$ years, have revealed significant reductions in CV morbidity/mortality with antihypertensive treatment. By contrast, several long-term interventional trials also have demonstrated J-curve phenomena for the relationships of achieved systolic BP (SBP),[3,9–11] diastolic BP (DBP)[12,13] and both[14] with CV morbidity/mortality in elderly hypertensive patients with various CV conditions, including coronary heart disease. Moreover, hypertension is also known to be linked to frailty in the elderly.[15,16] In Japan, the public Long-Term Care Insurance system provides services to disabled older adults who have been certified as requiring support (levels 1–2) or care (levels 1–5).[17,18] However, few studies have examined the association of BP with disability-free survival in community-dwelling elderly hypertensive patients. Therefore, we sought to determine the appropriate BP for elderly patients receiving antihypertensive treatment by examining the associations between baseline BP and the risk of incident disability or death.

METHODS

Subjects

The target area was a town with a population of ~30 000 in Ishikawa, Japan. The proportion of elderly people aged $\geqslant 65$ years in the total population was 19.6% (2010). The local government provides a public health center-based annual health check-up to these elderly subjects. In April 2008, of all 4050 community-dwelling uncertified elderly subjects aged $\geqslant 65$ years, 1091 supplied complete information at the time of their health check-ups. Of those subjects, 62.6% were hypertensive, defined as BP $\geqslant 140/90$ mm Hg or receiving current antihypertensive treatment ($n=683$). Among hypertensive subjects,

[1]Department of Geriatric Medicine, Kanazawa Medical University, Ishikawa, Japan and [2]School of Nursing, Kanazawa Medical University, Ishikawa, Japan
Correspondence: Professor S Morimoto, Department of Geriatric Medicine, Kanazawa Medical University, 1-1 Daigaku, Uchinada, Ishikawa 920-0293, Japan.
E-mail: shigeto@kanazawa-med.ac.jp
Received 15 November 2013; revised 30 November 2013; accepted 5 December 2013; published online 27 March 2014

84.8% were receiving antihypertensive treatment ($n=579$)[19] and were included in our study.

Baseline examinations

A self-administered questionnaire, which included medical history and time since the last meal,[20] was completed at baseline. The blood condition was defined as fasting if blood was collected more than 8 h after the last meal. Chronic kidney disease was defined as an estimated glomerular filtration rate, calculated using the modification of diet in renal disease equation with coefficients modified for Japanese patients,[21] of $<60\,ml\,min^{-1}\,1.73\,m^{-2}$. Diabetes mellitus was defined as fasting blood glucose $\geqslant 7.0\,mmol\,l^{-1}$ ($126\,mg\,dl^{-1}$), non-fasting glucose $\geqslant 11.1\,mmol\,l^{-1}$ ($200\,mg\,dl^{-1}$), HbA1c $\geqslant 6.5\%$ by a standardized method, or the use of hypoglycemic agents and/or insulin.[22] Dyslipidemia was defined as fasting serum total cholesterol $\geqslant 220\,mg\,dl^{-1}$, triglycerides $\geqslant 150\,mg\,dl^{-1}$, HDL cholesterol $<40\,mg\,dl^{-1}$, or use of the lipid-lowering agents.[23] Hyperuricemia was defined as serum uric acid $\geqslant 7.0\,mg\,dl^{-1}$ in men and $\geqslant 6.0\,mg\,dl^{-1}$ in women or the use of uric acid-lowering agents.[24] Hypoalbuminemia was defined as serum albumin $<4\,g\,dl^{-1}$.[25]

Measurements of baseline BP were performed based on the guidelines for the management of hypertension,[26] by trained observers using a mercury sphygmomanometer.

Analysis

The primary endpoint of the present study was the composite outcome of incident disability, defined as the first certification for any level of support/care need, or death. Support/care need was judged by the Regional Comprehensive Support Center (RCSC) of the local government, on the basis of the investigation form completed by interview by the RCSC staff and of the doctor's assessment form completed by the physician in charge.[17] We also examined the first disease causing the need for support/care need on the papers of all certificated persons, and we classified the diseases into four categories, namely cerebral events, falls/bone fractures, dementia/depression and other diseases. Baseline SBP and DBP were each classified into four classes (SBP: <120, 120–139, 140–159 and $\geqslant$160 mm Hg; DBP: <70, 70–79, 80–89 and $\geqslant$90 mm Hg).[3,9] The results for continuous variables in baseline clinical characteristics were compared using Mann–Whitney *U*-analysis. Discrete variables were compared by χ^2-analysis. Comparisons of data among the groups of SBP and DBP were performed by the Kruskal–Wallis test with Bonferroni's correction. Proportional hazards regression (Cox) models[27] were used to estimate the unadjusted hazard ratio (HR) of incident disability or death with 95% confidence intervals (CIs) by age, sex, risk factors shown in Table 1, and classes of SBP or DBP. Multivariate models were used to adjust for potential confounding factors at $P<0.20$.[28] Using Cox regression, the HR for each baseline BP (SBP: 140–159 mm Hg; DBP: 70–79 mm Hg) and the corresponding 95% CI were calculated. Data were analyzed using IBM-SPSS software (v. 18.0, IBM–SPSS, Chicago, IL, USA).

Ethical considerations

The study was formally approved by the Clinical Research Ethics Committee of Kanazawa Medical University. It was also approved by official agreement between the mayor of the town and us. We received baseline data and information of new onset of disability or death, which were irreversibly anonymized, during the follow-up period from the RCSC of the town.

RESULTS

Study population

Out of the 579 treated hypertensive elderly patients, nine moved out of the area during the four-year period and were also excluded. A total of 570 subjects (225 men and 345 women) were included in this analysis. Table 1 shows the baseline clinical characteristics of all of the patients at study entry. The mean ± s.d. age of subjects was 74.2 ± 6.1 years (65–94 years). The percentage of patients aged $\geqslant$75 years was 46.3% (Table 1).

Disability and death

A total of 77 subjects (33.8/1,000 person-years) either became disabled or died. These patients included 62 cases of incident disability (27.2/1,000 person-years) and 15 deaths without disability (6.6/1,000 person-years). Seven patients died after incident disability (3.1/1,000 person-years), and a total of 22 died (9.6/1,000 person-years) during the period (Table 1). Compared with patients with disability-free survival, patients with incident disability or death showed a significantly higher mean age and higher female sex rate (Table 1). The incidence rates of the composite outcome of incident disability and death for patients with baseline SBP <120, 120–139, 140–159 and $\geqslant$160 mm Hg were 45.9, 34.7, 19.7 and 75.6/1,000 person-years, respectively, while those for patients with baseline DBP <70, 70–79, 80–89 and $\geqslant$90 mm Hg were 37.5, 33.3, 33.3 and 32.9/1,000 person-years, respectively. The Kruskal-Wallis test revealed higher incidences of a past history of heart disease in the lower SBP groups and higher incidences of past histories of stoke, chronic kidney disease and diabetes mellitus in the lower DBP groups (Table 2).

Age, female sex, past history of stroke, past history of heart disease, chronic kidney disease, diabetes mellitus, hyperuricemia, and hypoalbuminemia were associated with the risk of incident disability or death in univariate analyses and were sequentially included in the final Cox proportional hazards regression model. The relationship between baseline SBP or DBP and the incidence of events is shown in Figure 1. After adjustment for these factors, the HR for disability or death over four years was significantly higher in subjects with baseline SBP <120 mm Hg (HR = 2.81, 95% CI = 1.15–6.82, $P=0.023$) and $\geqslant$160 mm Hg (HR = 4.32, 95% CI = 1.90–9.83, $P<0.001$), compared with subjects with baseline SBP of 140–159 mm Hg, which yielded the lowest incidence of events (Figure 1). After adjustment for the same factors, the HR for disability alone was also significantly higher both in subjects with baseline SBP <120 mm Hg (HR = 3.37, 95% CI = 1.18–9.60, $P=0.023$) and in those with baseline SBP $\geqslant$160 mm Hg (HR = 4.09, 95% CI = 1.03–8.16, $P=0.043$), compared with control subjects (Figure 1). Compared with the same control group, the HR for all-cause death was significantly higher in those with baseline SBP $\geqslant$160 mm Hg (HR = 6.10, 95% CI = 1.33–19.5, $P=0.017$) but not in those with <120 mm Hg. There was no difference in HR among each of the baseline DBP classes (Figure 1).

In the subgroup of patients aged $\geqslant$75 years, subjects with baseline SBP <120 mm Hg or $\geqslant$160 mm Hg had a significantly higher risk of all events (SBP <120 mm Hg: HR = 3.30, 95% CI = 1.18–9.21, $P=0.023$; SBP $\geqslant$160 mm Hg: HR = 4.41, 95% CI = 1.62–12.0, $P=0.004$) (Figure 2) and of incident disability alone (SBP <120 mm Hg: HR = 3.61, 95% CI = 1.12–12.0, $P=0.032$; SBP $\geqslant$160 mm Hg: HR = 3.67, 95% CI = 1.20–11.2, $P=0.022$), compared with subjects with baseline SBP of 140–159 mm Hg. There were no differences in HRs in the subgroup of patients aged 65–74 years (Figure 2).

Among the 62 disabled subjects, 11 patients were disabled owing to cerebral events, 15 owing to falls/bone fractures, 17 owing to dementia/depression, and 19 owing to other diseases. Of the 11 patients disabled owing to cerebral events, 10 did not have a previous history of stroke at the baseline examination. Conditional Cox hazard analysis revealed that the HR for disability owing to cerebral events was increased in subjects with baseline <120 mm Hg (HR = 27.3, 95% CI = 1.09–684, $P=0.044$), while that for disability owing to falls/bone fractures was increased in patients with SBP $\geqslant$160 mm Hg (HR = 25.0, 95% CI = 1.61–388, $P=0.021$), compared with the control group (Figure 3).

Table 1 Baseline characteristics of the total population with antihypertensive treatment

				Death			
	Total, n = *570*	*Disability or death,* n = *77*	*Disability,* n = *62*	*Total,* n = *22*	*Death with disability,* n = *7*	*Death without disability,* n = *15*	*Disability-free survival,* n = *493*
Demographics							
Age (years)	74.2 ± 6.1	79.5 ± 5.6***	80.6 ± 5.1***	78.1 ± 6.9**	84.3 ± 4.9***	75.1 ± 5.7	73.4 ± 5.7
Age > 75: *n* (%)	264 (46.3%)	63 (81.8%)***	55 (88.7%)***	15 (68.2%)#	7 (100%)**	8 (53.3%)	201 (40.8%)
Females: *n* (%)	345 (60.5%)	54 (70.1%)#	46 (74.2%)*	10 (45.5%)	2 (28.6%)	8 (53.3%)	291 (59.0%)
BMI ($kg\,m^{-2}$)	23.5 ± 3.2	23.5 ± 3.9	23.4 ± 3.8	23.0 ± 4.3	21.0 ± 3.2#	23.9 ± 4.5	23.5 ± 3.1
Complications							
Past history of stroke: *n* (%)	31 (5.5%)	8 (10.5%)#	4 (6.5%)	5 (22.7%)**	1 (14.3%)	4 (26.7%)**	23 (4.7%)
Past history of heart disease: *n* (%)	100 (17.9%)	23 (30.3%)**	20 (32.3%)**	4 (18.2%)	1 (14.3%)	3 (20.0%)	77 (15.6%)
Chronic kidney disease: *n* (%)	216 (37.9%)	37 (48.1%)#	33 (53.2%)*	7 (31.8%)	3 (42.9%)	4 (26.7%)	179 (36.3%)
Diabetes mellitus: *n* (%)	125 (21.9%)	23 (29.9%)#	22 (35.5%)*	4 (18.2%)	3 (42.9%)#	1 (6.7%)	102 (20.7%)
Dyslipidemia: *n* (%)	298 (52.3%)	43 (55.8%)	36 (58.1%)	11 (50.0%)	4 (57.1%)	7 (46.7%)	255 (51.7%)
Hyperuricemia: *n* (%)	114 (20.0%)	17 (22.1%)	12 (19.4%)	7 (31.8%)#	2 (28.6%)	5 (33.3%)#	97 (19.7%)
Hypoalbuminemia: *n* (%)	30 (5.3%)	12 (15.6%)***	9 (14.5%)***	7 (31.8%)***	4 (57.1%)***	3 (20.0%)*	18 (3.7%)
Blood pressure at entry							
Systolic (mm Hg)	137.2 ± 14.3	139.3 ± 16.4	137.6 ± 15.9	141.7 ± 16.7	132.0 ± 11.5	146.2 ± 17.1*	136.9 ± 13.9
< 120: *n* (%)	49 (8.6%)	9 (11.7%)*	8 (12.9%)*	2 (9.1%)	1 (14.3%)	1 (6.7%)	40 (8.1%)
120–139: *n* (%)	288 (50.5%)	40 (50.5%)*	35 (56.5%)*	10 (45.5%)	5 (71.4%)	5 (33.3%)	248 (50.3%)
140–159: *n* (%)[a]	190 (33.3%)	15 (19.5%)	11 (17.7%)	5 (22.7%)	1 (14.3%)	4 (26.7%)	175 (35.5%)
⩾160: *n* (%)	43 (7.5%)	13 (16.9%)***	8 (12.9%)**	5 (22.7%)**	0 (0.0%)	5 (33.3%)**	30 (6.1%)
Diastolic (mmHg)	78.4 ± 9.0	78.2 ± 9.4	77.3 ± 9.3	80.1 ± 8.5	76.0 ± 6.2	81.9 ± 8.9	78.4 ± 9.0
< 70: *n* (%)	80 (14.0%)	12 (15.6%)	11 (17.7%)	2 (9.1%)	1 (14.3%)	1 (6.7%)	68 (13.8%)
70–79: *n* (%)[b]	203 (35.6%)	27 (35.1%)	22 (35.5%)	8 (36.4%)	3 (42.9%)	5 (33.3%)	176 (35.7%)
80–89: *n* (%)	211 (37.0%)	28 (36.4%)	23 (37.1%)	8 (36.4%)	3 (42.9%)	5 (33.3%)	183 (37.1%)
⩾90: *n* (%)	76 (13.3%)	10 (13.0%)	6 (9.7%)	4 (18.2%)	0 (0.0%)	4 (26.7%)	66 (13.4%)

Abbreviation: BMI, body mass index.
Results are expressed as mean ± s.d., or *n* (%). Mann–Whitney *U*-analysis or χ^2-analysis were used. #$P<0.20$, *$P<0.05$, **$P<0.01$ and ***$P<0.001$ *vs.* group with disability-free survival.
[a]Reference SBP.
[b]Reference DBP.

Table 2 Baseline characteristics by each quartile of SBP and DBP pressure.

	SBP					*DBP*				
	< 120, n = *49*	*120–139,* n = *288*	*140–159,* n = *190*[a]	*⩾160,* n = *43*	*Kruskal–Wallis,* P-*value*	*< 70,* n = *80*	*70–79,* n = *203*[b]	*80–89,* n = *211*	*⩾90,* n = *76*	*Kruskal–Wallis,* P-*value*
Demographics										
Age (years)	73.3 ± 5.6	74.8 ± 6.2*	73.4 ± 5.7	75.4 ± 6.7#	*	75.6 ± 6.4	74.8 ± 6.3	73.8 ± 5.7#	72.5 ± 5.7**	*
Age > 75 years: *n* (%)	23 (46.9%)	140 (48.6%)#	78 (41.1%)	23 (53.5%)#		43 (53.8%)	100 (49.3%)	93 (44.1%)	28 (36.8%)#	#
Females: *n* (%)	29 (59.2%)#	168 (58.3%)#	122 (64.2%)	26 (60.5%)		48 (60.0%)	123 (60.6%)	130 (61.6%)	44 (57.9%)	
BMI ($kg\,m^{-2}$)	23.9 ± 2.7	23.2 ± 3.2#	23.7 ± 3.3	24.0 ± 3.3	#	23.3 ± 3.6	23.2 ± 3.2	23.8 ± 3.0*	23.9 ± 3.1#	#
Complications										
Past history of stroke: *n* (%)	4 (8.2%)	17 (5.9%)	8 (4.2%)	2 (4.7%)		2 (2.5%)	7 (3.4%)	19 (9.0%)*	3 (3.9%)	*
Past history of heart disease: *n* (%)	14 (28.6%)*	58 (20.1%)*	25 (13.2%)	3 (7.0%)	**	22 (27.5%)*	34 (16.7%)	33 (15.6%)	11 (14.5%)	#
Chronic kidney disease: *n* (%)	23 (45.9%)#	117 (40.6%)#	61 (32.1%)	15 (34.9%)	#	41 (51.3%)**	70 (34.5%)	71 (33.6%)	34 (44.7%)#	*
Diabetes mellitus: *n* (%)	10 (20.4%)	68 (23.6%)	39 (20.5%)	8 (18.2%)		28 (35.0%)*	49 (24.1%)	40 (19.0%)	8 (10.5%)*	**
Dyslipidemia: *n* (%)	26 (53.1%)	151 (52.4%)	101 (53.2%)	20 (46.5%)		43 (53.8%)	109 (53.7%)	106 (50.2%)	40 (52.6%)	
Hyperuricemia: *n* (%)	8 (16.3%)#	33 (11.5%)	18 (9.5%)	9 (20.9%)*	#	7 (8.8%)	26 (12.8%)	23 (10.9%)	12 (15.8%)	
Hypoalbuminemia: *n* (%)	3 (5.1%)	17 (5.9%)	7 (3.7%)	3 (7.9%)		8 (10.0%)#	9 (4.4%)	11 (5.2%)	2 (2.6%)	#

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.
Results are expressed as mean ± s.d., or *n* (%). Mann–Whitney *U*-analysis or χ^2-analysis was used.
[a]Reference SBP
[b]Reference DBP. Comparisons of data among classes of SBP and DBP were performed by Kruskal–Wallis test with Bonferroni's correction. #$P<0.20$, *$P<0.05$ and **$P<0.01$.

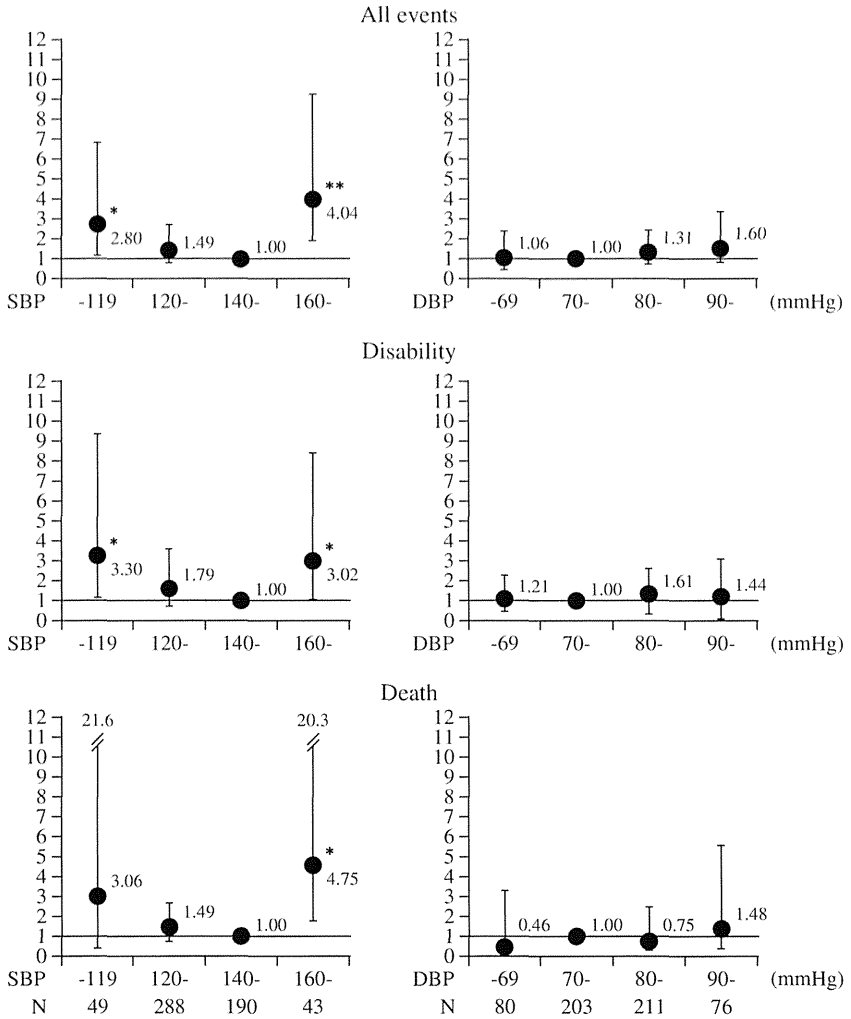

Figure 1 Relationship between baseline blood pressure (BP) and the hazard ratio of incident disability or death. Data are presented with relative risks and 95% confidence intervals with reference to patients with baseline systolic BP (SBP) of 140–159 mm Hg and patients with baseline diastolic BP (DBP) of 70–79 mm Hg. $*P<0.05$; $**P<0.01$.

DISCUSSION

The present study newly revealed an emerging profile of treated hypertension and the discontinuance of disability-free survival in community-dwelling elderly subjects. The advantages of the present study are as follows: Long-Term Care Insurance system certification is based on strictly established, uniform criteria throughout Japan,[17,18] and the included information enabled a very high follow-up rate in the present study (98.4%). Another advantage was that having information about the causal disease for incident disability enabled clarification of whether the risk of incident disability owing to particular causal diseases was higher in any of the SBP groups.

Practitioner's trial on the efficacy of antihypertensive treatment in elderly patients with hypertension II (PATE-Hypertension-II)[9] and ONTARGET[10] revealed that elderly patients with higher achieved BP ($\geqslant$160 mm Hg) had significantly higher incidences of CV events. The present study revealed that patients with baseline SBP$\geqslant$160 mm Hg had a significantly higher risk not only of total death and also for incident disability, compared with the control group (Figure 1). We also observed an association of baseline SBP$\geqslant$160 mm Hg with an increased risk of incident disability owing to falls/bone fractures (Figure 3). Although the precise reason for the association are not clear, one of the possible explanations is hypertension-induced development of white matter lesions,[29] which increase the risk for incident bone fracture in community-dwelling elderly subjects.[30] Moreover, a sub-analysis of Hypertension in the Very Elderly Trial revealed that sufficient reduction of BP in very old patients with SBP $\geqslant$160 mm Hg was associated with a significant reduction in fracture rate.[31] The precise mechanism for the association should be clarified in the future.

The present study clearly detected J-curve phenomena for the risk of incident disability or death, as well as for incident disability alone (Figure 1). The J-curve phenomenon appeared in patients aged $\geqslant$75 years but not in younger patients (Figure 2). The SBP range at the HR nadir of 140–159 mm Hg observed in the present study was somewhat higher than the target BP recommended for elderly patients aged $\geqslant$75 years by the Japanese treatment guidelines for hypertension, which include both using an intermediate target BP of $<$150/90 mm Hg and attempting to lower the patient's BP to $<$140/90 mm Hg if possible.[26] However, a lower target BP is not necessarily beneficial in elderly patients.[32] Indeed, in many large-scale clinical studies in elderly hypertensive patients aged $\geqslant$60 years, the mean BP achieved by antihypertensive treatment was 141–152/77–85 mm Hg.[2–8] Moreover,

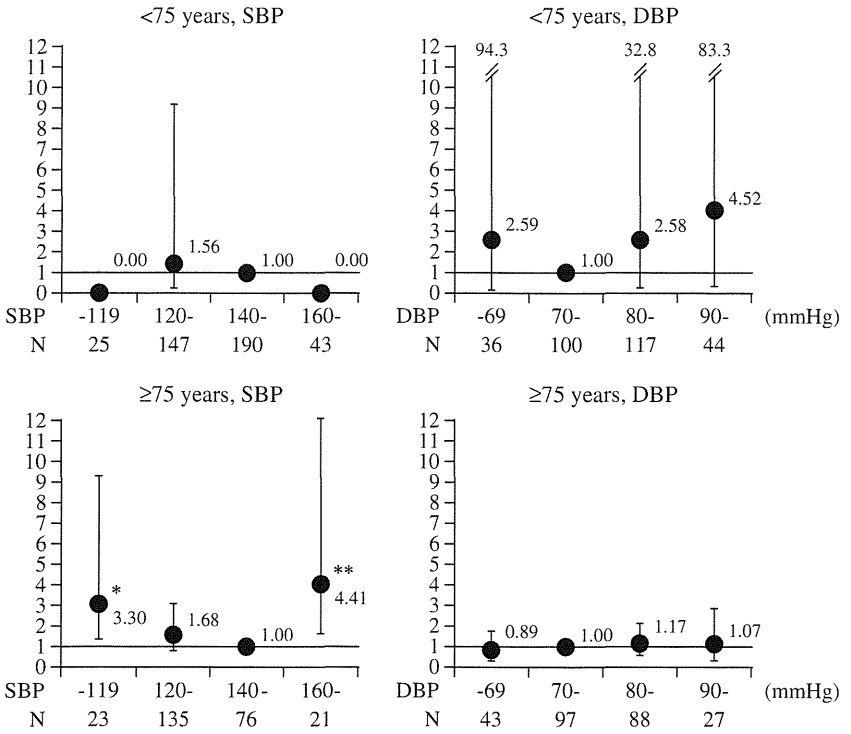

Figure 2 Relationship between baseline blood pressure (BP) and hazard ratio of incident disability or death in patients <75 years or ⩾75 years. Keys as in Figure 1.

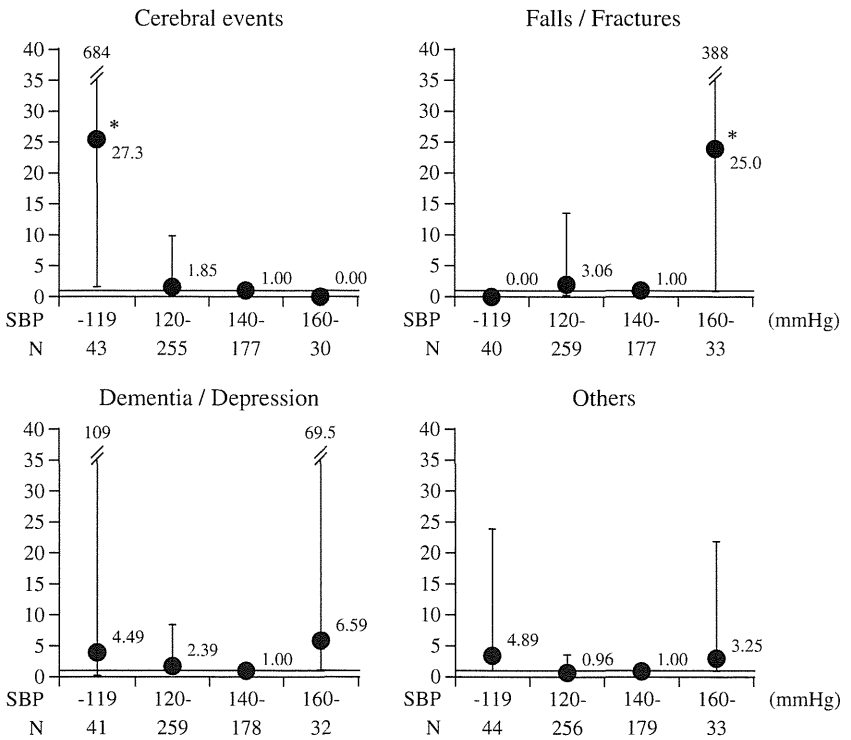

Figure 3 Relationship between baseline systolic blood pressure (SBP) and hazard ratio of incident disability according to the four categories of first causal disease for support/care need on doctor's assessment form. Keys as in Figure 1.

a sub-analysis of Systolic Hypertension in the Elderly Program (SHEP) (mean age 72 years) showed that participants whose in-trial SBP was lower than 160 mm Hg or 150 mm Hg experienced significant reductions in total stroke incidence compared with those with SBP higher than the respective thresholds, although the reduction of stroke incidence in those with SBP < 140 mm Hg was

not significant compared with that in those with SBP ⩾ 140 mm Hg,[33] indicating that reduction of stroke incidence could be achieved most effectively in those with in-trial SBP of 140–159 mm Hg. Furthermore, among the Japanese elderly hypertensive patients (⩾75 years) in the Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS), which compared the two-year effects of strict treatment to maintain SBP less than 140 mm Hg (group A) with those of mild treatment to maintain SBP between 140 and 160 mm Hg (group B), group B had a lower incidence of CV events compared with group A, although the difference was not significant.[34] In addition to these findings, elevated BP (⩾140 mm Hg) is not necessarily associated with a decreased survival rate in frail elderly subjects because elevated BP was independently associated with a lower risk of death (HR, 0.38) in subjects who could not complete a walk test (6 m), but it was associated with greater risk of mortality compared with subjects without elevated BP (HR, 1.35) among faster walkers ($\geqslant 0.8\ m\ s^{-1}$).[35] Because the mean age of patients certified with disability in the present study was 80.6 years (Table 1), all of these reports might be compatible to the present observation that patients with SBP of 140–159 mm Hg experienced the lowest risk for events.

PATE-Hypertension[3] and PATE-Hypertension II[9] demonstrated J-curve phenomena for CV morbidity/mortality in elderly patients (⩾75 years) with a J-curve point for SBP of <120 mm Hg, similar to that in the present study (Figures 1 and 2). A sub-analysis of ONTARGET also demonstrated a J-curve phenomenon for CV morbidity/mortality in high-risk patients with a mean age of 66 years, with a J-curve point for SBP of <130 mm Hg.[10] The Japanese Survey for Valsartan In Deployment (J-VALID) also demonstrated a significant systolic J-curve phenomenon, with a J-curve point for SBP of <120 mm Hg in elderly patients (⩾75 years).[11] J-curve phenomena in these studies were observed for cardiac events but not for stroke. In contrast, a sub-analysis of the International Verapamil SR-Trandolapril Study (INVEST) in patients with hypertension and coronary heart disease also showed J-curve phenomena for the primary endpoint in older age groups (70–<80 years, ⩾80 years) with SBP and DBP at the HR nadirs of 140 mm Hg and 70 mm Hg, respectively, for the oldest age group (⩾80 years).[14] The primary endpoint of INVEST included not only all-cause death and nonfatal myocardial infarction but also nonfatal stroke.[14] This result, as well as those of SHEP,[33] are partly compatible with our study, in which a J-curve phenomenon was observed for incident disability at least partly owing to cerebral events (Figure 3). In contrast, another sub-analysis of SHEP[12] and a sub-analysis of the Systolic Hypertension in Europe in patients with concomitant coronary heart disease[13] also demonstrated J-curve phenomena for the relationship of achieved DBP with J-curve points of <60 mm Hg and <70 mm Hg, respectively. However, there were no differences in HR among the baseline DBP classes in the present study. Nevertheless, the observations in these previous reports, as well as in the present study, indicate the importance of avoiding excessive BP reduction because low BP can often be related to the unexpected manifestation of a J-curve paradox in very elderly hypertensive subjects with underlying chronic debilitating illnesses.[36] Indeed, higher incidences of CV events and risk factors for CV were observed in the groups with lower SBP or DBP in the present study (Table 2).

This study had several limitations. First, the analyses performed in the present study could not address the causality of excess BP reduction in the increased risk of disability. The patients with baseline SBP <120 mm Hg might have originally been at high risk for frailty because SBP is known to decrease in years immediately before dementia onset in community-dwelling hypertensive elderly subjects.[37] The risk of excess BP reduction in very elderly hypertensive patients should be assessed in the future in randomized, controlled trials that compare disability-free survival between hypertensive very elderly patients whose SBP is controlled at higher levels than 120 mm Hg and patients whose SBP is sustained at <120 mm Hg. Second, in light of the single community model, care must be taken in interpreting the results of the present study, and further evaluation in multi-regional trials is needed. Third, stratified sampling of incident disability or death according to the kinds of antihypertensive drugs used, including renin–angiotensin blockers, is also needed in future studies because the renin–angiotensin system is thought to have a crucial role in aging and/or frailty.[38] Finally, because of the small number of normotensives and untreated hypertensives in the present study, precise analysis was statistically limited in these groups and should be examined in the future.

In conclusion, the present study clearly identified J-curve phenomena for the risk of incident disability or death in community-dwelling very elderly patients (⩾75 years) receiving antihypertensive treatment, indicating that having a low target BP could cause exacerbation of frailty in elderly patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This work was supported by Research Funding for Longevity Sciences from the National Center for Geriatrics and Gerontology (NCGG) Japan, Comprehensive Research on Aging and Health, the Ministry of Health, Labor and Welfare, and grants from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

1 Insua JT, Sacks HS, Lau TS, Lau J, Reitman D, Pagano D, Chalmers TC. Drug treatment of hypertension in the elderly: a meta-analysis. *Ann Intern Med* 1994; **121**: 355–362.
2 National Intervention Cooperative Study in Elderly Hypertensives Study Group. Randomized double-blind comparison of a calcium antagonist and a diuretic in elderly hypertensives. *Hypertension* 1999; **34**: 1129–1133.
3 Ogihara T. Practitioner's trial on the efficacy of antihypertensive treatment in the elderly hypertension (The PATE-Hypertension study) in Japan. *Am J Hypertens* 2000; **13**: 461–467.
4 Lindholm LH, Hansson L, Ekbom T, Dahlof B, Lanke J, Linjer E, Schersten B, Wester PO, Hedner T, de Faire U. Comparison of antihypertensive treatments in preventing cardiovascular events in elderly diabetic patients: results from the Swedish Trial in Old Patients with Hypertension-2. STOP Hypertension-2 Study Group. *J Hypertens* 2000; **18**: 1671–1675.
5 Wing LM, Reid CM, Ryan P, Beilin LJ, Brown MA, Jennings GL, Johnston CI, McNeil JJ, Macdonald GJ, Marley JE, Morgan TO, West MJ. A comparison of outcomes with angiotensin-converting-enzyme inhibitors and diuretics for hypertension in the elderly. *N Engl J Med* 2003; **348**: 583–592.
6 Lithell H, Hansson L, Skoog I, Elmfeldt D, Hofman A, Olofsson B, Trenkwalder P, Zanchetti A. The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J Hypertens* 2003; **21**: 875–886.
7 Lithell H, Hansson L, Skoog I, Elmfeldt D, Hofman A, Olofsson B, Trenkwalder P, Zanchetti A. The Study on COgnition and Prognosis in the Elderly (SCOPE); outcomes in patients not receiving add-on therapy after randomization. *J Hypertens* 2004; **22**: 1605–1612.
8 Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008; **358**: 1887–1898.
9 Ogihara T, Matsuoka H, Rakugi H. Practitioner's trial on the efficacy of antihypertensive treatment in elderly patients with hypertension II (PATE-hypertension II study) in Japan. *Geriatr Gerontol Int* 2011; **11**: 414–421.
10 Sleight P, Redon J, Verdecchia P, Mancia G, Gao P, Fagard R, Schumacher H, Weber M, Böhm M, Williams B, Pogue J, Koon T, Yusuf S. ONTARGET investigators. Prognostic value of blood pressure in patients with high vascular risk in the Ongoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial study. *J Hypertens* 2009; **27**: 1360–1369.

11 Yamazaki T, Kohro T, Chujo M, Ishigaki M, Hashimoto T. The occurrence rate of cerebrovascular and cardiac events in patients receiving antihypertensive therapy from the post-marketing surveillance data for valsartan in Japan (J-VALID). *Hypertens Res* 2013; **36**: 140–150.
12 Somes GW, Pahor M, Shorr RI, Cushman WC, Applegate WB. The role of diastolic blood pressure when treating isolated systolic hypertension. *Arch Intern Med* 1999; **159**: 2004–2009.
13 Fagard RH, Staessen JA, Thijs L, Celis H, Bulpitt CJ, de Leeuw PW, Leonetti G, Tuomilehto J, Yodfat Y. On-treatment diastolic blood pressure and prognosis in systolic hypertension. *Arch Intern Med* 2007; **167**: 1884–1891.
14 Denardo SJ, Gong Y, Nichols WW, Messerli FH, Bavry AA, Cooper-Dehoff RM, Handberg EM, Champion A, Pepine CJ. Blood pressure and outcomes in very old hypertensive coronary artery disease patients: an INVEST substudy. *Am J Med* 2010; **123**: 719–726.
15 Wang L, van Belle G, Kukull WB, Larson EB. Predictors of functional change: A longitudinal study of nondemented people aged 65 and older. *J Am Geriatr Soc* 2002; **50**: 1525–1534.
16 Bastos-Barbosa RG, Ferriolli E, Coelho EB, Moriguti JC, Nobre F, da Costa Lima NK. Association of frailty syndrome in the elderly with higher blood pressure and other cardiovascular risk factors. *Am J Hypertens* 2012; **25**: 1156–1161.
17 Tsutsui T, Muramatsu N. Care-needs certification in the long-term care insurance system of Japan. *J Am Geriatr Soc* 2005; **53**: 522–527.
18 Tsutsui T, Muramatsu N. Japan's universal long-term care system reform of 2005: costs and realizing a vision. *J Am Geriatr Soc* 2007; **55**: 1458–1463.
19 Koizumi Y, Hamazaki Y, Okuro M, Iritani O, Yano H, Higashikawa T, Iwai K, Morimoto S. Association between hypertension status and the screening test for frailty in elderly community-dwelling Japanese. *Hypertens Res* 2013; **36**: 639–644.
20 Saito I, Kokubo Y, Yamagishi K, Iso H, Inoue M, Tsugane S. Diabetes and the risk of coronary heart disease in the general Japanese population: the Japan Public Health Center-based prospective (JPHC) study. *Atherosclerosis* 2011; **216**: 187–191.
21 Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, Yamagata K, Tomino Y, Yokoyama H, Hishida A, on behalf of the collaborators developing the Japanese equation for estimated GFR. Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis* 2009; **53**: 982–992.
22 Kuzuya T, Nakagawa S, Satoh J, Kanazawa Y, Iwamoto Y, Kobayashi M, Nanjo K, Sasaki A, Seino Y, Ito C, Shima K, Nonaka K, Kadowaki T. Committee of the Japan Diabetes Society on the diagnostic criteria of diabetes mellitus. Report of the Committee on the classification and diagnostic criteria of diabetes mellitus. *Diabetes Res Clin Pract* 2002; **55**: 65–85.
23 Bando Y, Kanehara H, Aoki K, Katoh K, Toya D, Tanaka N. Characteristics of undiagnosed diabetes mellitus in a population undergoing health screening in Japan: target populations for efficient screening. *Diabetes Res Clin Pract* 2009; **83**: 341–346.
24 Nagahama K, Inoue T, Iseki K, Touma T, Kinjo K, Ohya Y, Takishita S. Hyperuricemia as a predictor of hypertension in a screened cohort in Okinawa, Japan. *Hypertens Res* 2004; **27**: 835–841.
25 Sullivan DH, Roberson PK, Bopp MM. Hypoalbuminemia 3 months after hospital discharge: significance for long-term survival. *J Am Geriatr Soc* 2005; **53**: 1222–1226.
26 Japanese Society of Hypertension Committee. The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2009). *Hypertens Res* 2009; **32**: 3–107.
27 Cox DR. Regression models and life tables. *J R Statist Soc (B)* 1972; **34**: 187–220.
28 Concato J, Feinstein AR, Holford TR. The risk of determining risk with multivariable models. *Ann Intern Med* 1993; **118**: 201–210.
29 Fukuda H, Kitani M. Differences between treated and untreated hypertensive subjects in the extent of periventricular hyperintensities observed on brain MRI. *Stroke* 1995; **26**: 1593–1597.
30 Corti MC, Baggio G, Sartori L, Barbato G, Manzato E, Musacchio E, Ferrucci L, Cardinali G, Donato D, Launer LJ, Zambon S, Crepaldi G, Guralnik JM. White matter lesions and the risk of incident hip fracture in older persons: results from the progetto veneto anziani study. *Arch Intern Med* 2007; **167**: 1745–1751.
31 Peters R, Beckett N, Burch L, de Vernejoul MC, Liu L, Duggan J, Swift C, Gil-Extremera B, Fletcher A, Bulpitt C. The effect of treatment based on a diuretic (indapamide) +/- ACE inhibitor (perindopril) on fractures in the Hypertension in the Very Elderly Trial (HYVET). *Age Ageing* 2010; **39**: 609–616.
32 August P. Initial treatment of hypertension. *N Engl J Med* 2003; **348**: 610–616.
33 Perry HM Jr, Davis BR, Price TR, Applegate WB, Fields WS, Guralnik JM, Kuller L, Pressel S, Stamler J, Probstfield JL. Effect of treating isolated systolic hypertension on the risk of developing various types and subtypes of stroke: the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 2000; **284**: 465–471.
34 JATOS Study Group. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS). *Hypertens Res* 2008; **31**: 2115–2127.
35 Odden MC, Peralta CA, Haan MN, Covinsky KE. Rethinking the association of high blood pressure with mortality in elderly adults: the impact of frailty. *Arch Intern Med* 2012; **172**: 1162–1168.
36 Angeli F, Reboldi G, Verdecchia P. Hypertension and the J-curve phenomenon: implications for tight blood pressure control. *Hypertens Res* 2013; **36**: 109–111.
37 Skoog I, Lernfelt B, Landahl S, Palmertz B, Andreasson LA, Nilsson L, Persson G, Odén A, Svanborg A. 15-year longitudinal study of blood pressure and dementia. *Lancet* 1996; **347**: 1141–1145.
38 Abadir PM. The frail renin-angiotensin system. *Clin Geriatr Med* 2011; **27**: 53–65.

Sleep apnea in the elderly

Masashi Okuro and Shigeto Morimoto

Purpose of review
Sleep apnea syndrome (SAS) in the elderly presents varied clinical symptoms and also has many complications. Moreover, there are many hospital departments related to these symptoms. This article uses literature to provide an outline on SAS observed in the elderly.

Recent findings
SAS sufferers often have complications with so-called lifestyle-related diseases, such as hypertension, hyperlipidemia, diabetes mellitus and metabolic syndrome. These symptoms, along with SAS, recede as a result of continuous positive airway pressure treatment. Some have also reported recession of depression symptoms and delay in deterioration of cognitive functions.

Summary
The elderly tends to develop SAS through coexistence of chronic respiratory organ disorders, increase in upper airway collapse, strokes, cardiovascular diseases, hypertension, diabetes mellitus and other physiological anatomical changes that accompany aging. However, judgment on the severity and effects regarding prognosis by each remedy used in the diagnosis and treatment of SAS in the elderly is still being developed, and it is considered necessary to accumulate more evidence and establish new standards.

Keywords
continuous positive airway pressure, elderly, Epworth sleepiness scale, international classification of sleep disorders 3, sleep apnea syndrome

INTRODUCTION

It is assumed that the elderly tends to develop sleep apnea syndrome (SAS) through coexistence of chronic respiratory organ disorders, increase in upper airway collapse, stroke [1▪], cardiovascular diseases [2–5], hypertension [6], diabetes mellitus [7] and so forth as physiological and anatomical changes in concurrence with aging. However, elderly SAS sufferers very seldom visit medical institutes for sleep-disordered breathing, as symptoms are not always apparent due to lower snoring volume, weight loss and fewer consequences of daytime somnolence. Therefore, the diagnosis rate is low and the problem is often overlooked. It is also believed that there are many cases of complications with other sleep disorders.

SAS was proposed by Professor Guilleminault [8], in 1976, who established its treatment system under diagnosis with polysomnogram (PSG). Although it is classified into obstructive, central and combined, SAS usually refers to obstructive SAS (OSAS), which has the highest occurrence. OSAS often happens to people who snore loudly, and the disease conditions include effort to breathe during apnea, which occurs in concurrence with sleep, as well as paradoxical movements in the thorax and abdominal wall. OSAS often occurs in people with narrowed upper airways due to obesity, and people with small, narrow chins. SAS is diagnosed when air current through the nose and mouth stops for 10 s or longer at a time (respiratory arrest) at a frequency of five or more times an hour [9]. Severity is indicated by apnea–hypopnea index on the basis of apnea count per hour. When breathing stops, SAS sufferers have difficulty breathing, become oxygen deficient and have their sleep interrupted many times during the night. However, the person himself or herself is often not aware of their state, and the subjective symptoms are usually excessive sleepiness and fatigue during the day. Frequent interruptions caused by an oxygen deficiency result in poor quality sleep, which impacts upon the sufferers' work efficiency due to reduced memory and

Department of Geriatric Medicine, Kanazawa Medical University, Ishikawa, Japan

Correspondence to Masashi Okuro, Department of Geriatric Medicine, Kanazawa Medical University, 1–1 Daigaku, Uchinadamachi, Kahoku-gun, Ishikawa Prefecture, Japan 920–0293. Tel: +81 76 286 2211 x6512; fax: +81 76 286 6053; e-mail: okuro@kanazawa-med.ac.jp

Curr Opin Psychiatry 2014, 27:472–477
DOI:10.1097/YCO.0000000000000105

KEY POINTS

- The elderly tend to develop SAS because of complications with the physiological and anatomical changes that accompany aging.
- SAS presents various different clinical symptoms. There are also many hospital departments that are related to these symptoms.
- An effective treatment method for SAS is nasal CPAP therapy.
- Judgment on the severity and effects of each remedy regarding prognosis in diagnosis and treatment of SAS in the elderly has not been fully established, and both the accumulation of evidence and establishment of new standards are necessary.

concentration skills accompanying hypersomnia and tiredness during the day. Such a state may result in the sufferer falling asleep at the wheel or causing serious accidents through the mistaken operation of a machine. Those who are attacked by hypersomnia during the day should suspect sleep disorders, such as SAS, and actively seek the help of a specialist. SAS also presents various different clinical symptoms relating to many hospital departments.

This article uses literature to provide an outline on SAS in the elderly.

PATHOLOGY

It is known that the frequency of SAS increases in concurrence with aging [10–12]. According to a sleep heart health study (SHHS) in the United States, 46% or more had apnea–hypopnea index 5 or higher in a sample of 6132 adults. Fifty-five percent of this sample was 65 years or older [13].

As people age, deterioration in upper airway muscle activities, pharynx dilator reflex and lung capacity, as well as extension in upper airway length, etc. has been observed. In particular, the pharynx lower and upper airway extends as people age. These airways tend to close up to accompany physiological reduction in lung capacity. It is assumed that changes in upper airway resistance and increased nocturnal awakening increase the instability of respiratory control. It is also possible that edentulous jaw and so forth are also involved in stricture of the upper airway [14].

DIAGNOSIS

Subjective symptoms include discomfort or headache upon awakening, snoring, night sweat, nocturia, erectile dysfunction and sleepiness during the day.

In diagnosis, sleep conditions, sleepiness during the day and so forth are important and family members should also be interviewed in addition to the sufferer during history taking. As a method to evaluate the subjective symptoms for sleepiness, Epworth sleepiness scale is used, and it is considered that sleepiness is severe if the total score of the evaluation items is 11 or higher (Table 1) [15].

As there are no standards or guidelines regarding the diagnosis and treatment of SAS in the elderly, the fact is that the guidelines for general adults are being applied at present. In November 2012, the judgment rules for PSG tests by the American Academy of Sleep Medicine were revised, and it was decided that the Japanese Society of Sleep Research would also conform to the judgment rules of the American Academy of Sleep Medicine as shown in Table 2 in judgment of sleep, apnea and so forth [16,17,18▪,19].

The diagnostic criteria for obstructive sleep apnea (OSA) in adults by International Classification of

Table 1. Epworth sleepiness scale

Situation	Chance of dozing			
Sitting and reading	0	1	2	3
Watching television	0	1	2	3
Sitting inactive in a public place (theater or meeting)	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after lunch (with no alcohol)	0	1	2	3
In a car, while stopped in traffic	0	1	2	3

Adapted from [15].

Table 2. Judgment rules for through-the-night polysomnogram by the American Academy of Sleep Medicine (version 2) [16]

Apnea shall be diagnosed when all of the following standards are satisfied with thermistor:

When the maximum amplitude for temperature sensor decreases by 90% or larger from the standard value,

the event duration shall be at least 10 s or longer,

At least 90% of the events shall satisfy the apnea amplitude standard.

Hypopnea shall be diagnosed when all of the following standards are satisfied in check with a pressure sensor (1, 2+3a, 4a or 1, 2+3b, 4b):

1. The duration of hypopnea is at least 10 s.
2. At least 90% satisfy the amplitude deterioration standard for hypopnea during the event duration.

<Alternative standard>

3a. Nose pressure signal (or another alternative hypopnea sensor) amplitude decreases by 30% or larger from the standard.

4a. Deterioration of 4% or larger from the oxygen saturation before the event.

<Recommended standard>

3b. Nose pressure signal (or another alternative hypopnea sensor) amplitude decreases by 30% or larger from the standard.

4b. Deterioration of 3% or larger from the oxygen saturation before the event or arousal concurs.

Sleep Disorders 3rd edition [20] are shown in Table 3. Breathing events are checked by through-the-night PSG tests implemented by medical institutes specializing in sleep, as well as simple tests by nonspecialist medical institutes, and SAS is diagnosed when there are five or more breathing events per hour, if the sufferer has symptoms or an underlying disease, and when there are 15 or more breathing events per hour, if the sufferer is free of symptoms or underlying diseases.

METHOD OF TREATMENT

Although there is no remedy that completely cures SAS, the first selection, which is the most effective remedy, is nasal continuous positive airway pressure (CPAP) therapy. The treatment system for this method tries to remove apnea by continuously running air from a mask attached to the nose during sleep and applying pressure so that the airway is expanded and obstruction is prevented [21,22▪,23].

Table 3. Diagnostic criteria for obstructive sleep apnea in adults (International Classification of Sleep Disorders-3) [20]

(A and B) or C satisfies the criteria.

A. The presence of one or more of the following:

1. The patient complains of sleepiness, nonrestorative sleep, fatigue or insomnia symptoms.
2. The patient wakes with breath holding, gasping or choking.
3. The bed partner or other observer reports habitual snoring, breathing interruptions or both during the patient's sleep.
4. The patient has been diagnosed with hypertension, a mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, arterial fibrillation or type II diabetes mellitus.

B. Polysomnography or OCST[a] demonstrates:

1. Five or more predominantly obstructive respiratory events[b]

(obstructive and mixed apneas, hypopneas or RERAs[c]) per hour of sleep during a PSG or per hour of monitoring (OCST)[a].

OR

C. PSG or OCST[a] demonstrates:

1. Fifteen or more predominantly obstructive respiratory events

(apneas, hypopneas, or RERAs)[c] per hour of sleep during a PSG or per hour of monitoring (OCST)[a].

OCST, *out-of-center sleep testing*; PSG, *polysomnography*; RERAs, *respiratory effort-related arousal*.

[a]OCST commonly underestimates the number of obstructive respiratory events per hour as compared with polysomnography because actual sleep time, as determined primarily by electroencephalography, is often not recorded.

The term respiratory event index may be used to denote event frequency on the basis of monitoring time rather than total sleep time.

[b]Respiratory events defined according to the most recent version of the American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated Events.

[c]RERAs and hypopnea events on the basis of arousals from sleep cannot be scored using OCST because arousals by electroencephalography criteria cannot be identified.

When a nose mask is used without problem, effects are most apparent on sufferers with severe subjective symptoms, such as sleepiness during the day, headaches in the morning and nocturia. There have also been reports on improvement in hypertension and heart failure that are considered to be complications related to SAS [24].

Although the general remedy for OSA is CPAP, there are a notable number of sufferers who are unable to tolerate CPAP. Upper airway stimulation therapy for OSA is a method that involves sending electric stimulation pulse to the hypoglossal nerve using a stimulation lead wire from a device implanted in the chest, in an attempt to prevent airway collapse during breathing and maintain airway persistence. Breathing is monitored using another detection lead wire connected to intercostal muscle. According to a study examining the clinical safety and effectiveness of upper airway stimulation therapy, the existence of alternative choices for sufferers who cannot tolerate CPAP can be anticipated [25].

Dental equipment (mouthpiece) is used for other sufferers, including sufferers with snore-type or light SAS and sufferers who cannot continue CPAP therapy because of discomfort. The mouthpiece is prepared by a dentist to suit each individual sufferer so that the lower jaw and tongue are pushed forward during sleep. In addition, some sufferers undergo a surgery called uvulopalatopharyngoplasty to expand the upper airway [26,27].

However, it is important that SAS sufferers also improve their ongoing daily lifestyle. SAS sufferers often have complications with the so-called lifestyle-related diseases, such as hypertension, hyperlipemia, diabetes and metabolic syndrome, and are in need of losing weight [28,29]. However, slender SAS sufferers whose cause of SAS is considered to be the shape of the face or jaw will not benefit from weight loss. It is also necessary to quit smoking as smoking causes inflammation of laryngopharynx and worsens SAS. Avoiding drinking, overwork and use of tranquilizers that worsen the condition, as well as sleeping on one's side are also effective in preventing the tongue root from sagging.

COMPLICATIONS AND PROGNOSIS

The significance of SAS treatment in the elderly has been a daily clinical problem. A prospective observational study on the elderly revealed that people with severe apnea, who did not receive CPAP therapy, had higher possibilities of death by cardiovascular disorders compared with people without apnea. The study results by Martínez-García *et al.* [30] indicated a possibility that the risks of death by cardiovascular disorders can be reduced in the elderly with snoring and sleep apnea by introducing a proper sleep test and CPAP therapy.

The connection between SAS and hypertension [31], cerebral infarction, heart diseases and sudden deaths is being revealed by many study reports [32]. There is a report in which CPAP therapy was conducted on sufferers with both SAS and refractory hypertension for 3 months and a significant decrease in diastolic pressure and nocturnal blood pressure was observed. In a daily diagnosis and treatment, blood pressure may decrease in refractory hypertension sufferers by not only increasing the depressor drug, but also by considering the existence of comorbid disorders, such as sleep apnea, that may affect the blood pressure and by providing the corresponding treatment [33].

There are also reports in which it was directly shown in human cardiac insufficiency sufferers that OSAS with upper airway obstruction reduced cardiac output. Although the cardiac output decreased by 6.8% on average during apnea in obstructive pattern, it increased by 2.6% on average in the central pattern. In addition, an examination of which sufferers decrease in cardiac output occurred through multivariate analysis on apnea with obstructive pattern indicated that there were cases with reduced left ventricular ejection fraction, cases with long periods of apnea and cases with reduced oxygen concentration due to apnea. It is considered that this study result indicates the significance of sleep apnea combined with heart failure and that it is a meaningful study that indicated which sufferers should start and continue positive pressure therapy [34].

In past reports, relevance between SAS and cerebrovascular diseases had been observed in men, but there were no studies that targeted women alone. A report by Campos-Rodriquez *et al.* [35] revealed that there was relevance between SAS and brain infarction or coronary artery diseases, which reduce the life activity in women, and indicated the significance in screening and treatment of sleep apnea in women.

The American Heart Association and the American Stroke Association revised their stroke recurrence prevention guidelines in sufferers with a history of stroke and transient ischemic attack. The stroke recurrence prevention guidelines emphasized the importance of blood pressure and lipid management and also mentioned the usefulness of intervention in lifestyle. On the basis of the facts that the disease rate for SAS is high in sufferers with ischemic stroke or transient ischemic attack, and that there is evidence the outcome is improved in the general population by treatment on SAS, a new proposal was

made on sleep apnea that sleep test can be considered for these sufferers (class IIb, evidence level B) [36▪▪].

Aspiration often arises as an issue for the elderly. In addition to high risks of aspiration of expectoration into airways or lungs during sleep, it had been indicated that the possibility of pneumonia was higher due to the effects of sleep disorder on the immune system. An observational study using the national insurance database examined the relevance between sleep apnea and risks of pneumonia. The results indicate increased risks for adult sufferers of SAS compared with people without SAS symptoms. A comparison of risks for pneumonia after adjustment of various factors related to pneumonia risk showed a 19% increase in pneumonia risk in the SAS group compared with the control group (hazard ratio after adjustment 1.19, 95% confidence interval 1.08–1.30). In addition, increase in risk was larger in sufferers using CPAP with the value 1.32 (same as above, 1.12–1.55), whereas the hazard ratio for sufferers who were intolerant of CPAP was 1.15 (same as above, 1.04–1.27) [37].

There is a report that claims depression receded in 60% of sufferers when CPAP therapy was conducted for disorders other than cerebrovascular disorders. This indicates that SAS can be a cause of depression. In addition, improvement in depression symptoms is not observed in cases in which sleepiness during the day continues even after CPAP therapy. That is, it can be a clinical symptom that the depression is not caused by SAS. Although this study was purely observational, the results of CPAP intervention tests with a good design are anticipated in order to indicate clearer relevance between SAS and depression symptoms [38].

Improvement in blood pressure, subcutaneous fat and metabolic syndrome was observed in a 3-month period of CPAP therapy for SAS. This result indicates the possibility that sleep apnea itself could be a cause of hypertension, subcutaneous fat and metabolic syndrome. Although the study result by Sharma *et al.* [39] does not apply to all sufferers of sleep apnea, it is considered necessary for clinical doctors to apply a multilateral approach on sufferers with hypertension and metabolic syndrome in addition to drug treatment with depressors, statin and so forth with consideration of snoring and apnea at night.

OSAS is said to be related to dementia. It was indicated that repeated apnea at night in the elderly entailed the risk of reducing cognitive functions. It was also reported that OSAS delayed the deterioration in cognitive functions of sufferers with light-to-medium cases of Alzheimer disease. It is indicated that the continuous treatment of SAS in the elderly is necessary. On the basis of these research results, it is also considered necessary that general diagnosis and treatment should be provided while keeping in mind the existence of SAS as a primary method for prevention of dementia in the elderly [40–42,43▪▪].

CONCLUSION

Although the frequency of SAS increases as the person ages, there are also many areas for which the conclusion discussed above has not been reached. In addition, insomnia is observed with high frequency in the elderly as an age-related change. Although it is considered that they often visit psychiatry departments for nocturnal awakening and poor quality sleep, SAS symptoms may worsen with an increase in frequency of breathing events, such as apnea and hypopnea, and extension of their duration due to breathing adjustment function deterioration during sleep caused by central nervous system depression effect, as well as muscular relaxation effect of the drugs on groups of muscles related to airways and breathing, if sleeping drugs are prescribed readily without special consideration of SAS. As a result, they may fall into a vicious cycle of intensified insomnia and function impairment during the day. Determination of the severity and prognosis of each therapy is still insufficient regarding diagnosis and treatment of SAS in the elderly, and the accumulation of evidence and establishment of new standards are considered necessary.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- ▪ of special interest
- ▪▪ of outstanding interest

1. ▪ Camilo MR, Sander HH, Eckeli AL, *et al.* SOS score: an optimized score to screen acute stroke patients for obstructive sleep apnea. Sleep Med 2014; 14:192–200.

The Sleep Obstructive apnea score optimized for Stroke (SOS score) administered to relatives of stroke patients is a useful tool to screen for OSA and may decrease the need for polysomnography in acute stroke setting.

2. Khan MS, Bawany FI, Khan A, *et al.* Risk assessment for obstructive sleep apnea and anxiety in a Pakistani population with coronary artery disease sleep breath 2014. [Epub ahead of print]
3. Surani SR. Diabetes, sleep apnea, obesity and cardiovascular disease: why not address them together? World J Diabetes 2014; 5:381–384.
4. Tosur Z, Green D, De Chavez PJ, *et al.* The association between sleep characteristics and prothrombotic markers in a population-based sample: Chicago Area Sleep Study. Sleep Med 2014; 14:155–160.
5. Kendzerska T, Gershon AS, Hawker G, *et al.* Obstructive sleep apnea and risk of cardiovascular events and all-cause mortality: a decade-long historical cohort study. PLoS Med 2014; 11:e1001599.

6. Parati G, Lombardi C, Hedner J, *et al.* Recommendations for the management of patients with obstructive sleep apnoea and hypertension. Eur Respir J 2013; 41:523–538.
7. Bonsignore MR, Borel A-L, Machan E, Grunstein R. Sleep apnoea and metabolic dysfunction. Eur Respir Rev 2013; 22:353–364.
8. Guilleminault C, Tilkian A, Dement WC. The sleep apnea syndromes. Annu Rev Med 1976; 27:465–484.
9. American Academy of Sleep Medicine Task Force. The Report of an American Academy of Sleep Medicine Task Force: Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999; 22:667–689.
10. Tishler PV, Larkin EK, Schluchter MD, *et al.* Incidence of sleep-disordered breathing in an urban adult population: the relative importance of risk factors in the development of sleep-disordered breathing. JAMA 2003; 289:2230–2237.
11. Zamarro C, Gude F, Otero Y, *et al.* Prevalence of sleep disordered breathing and sleep apnea in 50- to 70- year- old individuals. Respiration 1999; 66:317–322.
12. Bixler EO, Vgontzas AN, Ten Have T, *et al.* Effects of age on sleep apnea in men: I. Prevalence and severity. Am J Respir Crit Care Med 1998; 157:144–148.
13. Nieto F, Young T, Lind B, *et al.* Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. JAMA 2000; 283:1829–1836.
14. Malhotra A, Huang Y, Fogel R, *et al.* Aging influences on pharyngeal anatomy and physiology: the predisposition to pharyngeal collapse. Am J Med 2006; 119:72.
15. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991; 14:540–545.
16. Berry RB, Budhiraja R, Gottlieb DJ, *et al.* American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications version 2.0. Illinois: American Academy of Sleep Medicine; 2012.
17. Grigg-Damberger MM. The AASM scoring manual four years later. J Clin Sleep Med 2012; 8:323–332.
18. ▪ Rosenberg RS, Van Hout S. The American Academy of Sleep Medicine Inter-scorer Reliability program: respiratory events. J Clin Sleep Med 2014; 10:447–454.

This study demonstrated excellent agreement among a large sample of scorers for epochs with no respiratory events. Agreement for some type of event was good, but disagreements in scoring of apnea vs. hypopnea and type of apnea were common. A limitation of the analysis is that most of the records had normal breathing. A review of controversial events yielded no consistent bias that might be resolved by a change of scoring rules.

19. Rosenberg RS, Van Hout S. The American Academy of Sleep Medicine inter-scorer reliability program: sleep stage scoring. J Clin Sleep Med 2013; 9:81-87.
20. The International Classification of Sleep Disorders: ICSD3, Diagnostic and Coding Manual. 3rd ed. Darien, Illinois: American Academy of Sleep Medicine; 2013.
21. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnea by continuous positive airway pressure applied through the nares. Lancet 2013; 1:862 L-865.
22. ▪ Young D, Collop N. Advances in the treatment of obstructive sleep apnea. Curr Treat Options Neurol 2014; 16:305.

This article focuses on the treatment of OSA, using the most recent available data.

23. Anandam A, Patil M, Akinnusi M, *et al.* Cardiovascular mortality in obstructive sleep apnoea treated with continuous positive airway pressure or oral appliance: an observational study. Respirology 2013; 18:1184–1190.
24. Kaneko Y, Floras JS, Usui K, *et al.* Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Eng J Med 2003; 348:1233–1241.
25. Strollo PJ Jr, Soose RJ, Maurer JT, *et al.* Upper-airway stimulation for obstructive sleep apnea. N Engl J Med 2014; 370:139–149.
26. Ankichetty S, Wong J, Chung F. A systematic review of the effects of sedatives and anesthetics in patients with obstructive sleep apnea. J Anaesthesiol Clin Pharmacol 2011; 27:447–458.
27. Chabolle F, de Dieuleveult T, Cabanes J, *et al.* Long-term results of surgical pharyngectomy (uvulo-palato-pharyngoplasty) versus office CO2 laser (L.A.U.P.) for the treatment of uncomplicated snoring. Ann Otolaryngol Chir Cervicofac 1998; 115:196–201.
28. Bun Leong W, Banerjee D, Nolen M, *et al.* Hypoxemia and glycemic control in type 2 diabetes mellitus with extreme obesity. J Clin Endocrinol Metab 2014; E1–E5.
29. Surani SR. Diabetes, sleep apnea, obesity and cardiovascular disease: why not address them together? World J Diabetes 2014; 5:381–384.
30. Martinez-García MA, Campos-Rodriguez F, Catalán-Serra P, *et al.* Cardiovascular mortality in obstructive sleep apnea in the elderly: role of long-term continuous positive airway pressure treatment: a prospective observational study. Am J Respir Crit Care Med 2012; 186:909–916.
31. Bakker JP, Edwards BA, Gautam SP, *et al.* Blood pressure improvement with continuous positive airway pressure is independent of obstructive sleep apnea severity. J Clin Sleep Med 2014; 10:365–369.
32. Morimoto S, Okaishi K, Okuro M, *et al.* Sleep apnoea syndrome as a risk for mortality in elderly in patients. J Int Med Res 2012; 40:601–611.
33. Martínez-García MA, Capote F, Campos-Rodríguez F, *et al.* Spanish Sleep Network. Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial. JAMA 2013; 310:2407–2415.
34. Yumino D, Kasai T, Kimmerly D, *et al.* Differing effects of obstructive and central sleep apneas on stroke volume in patients with heart failure. Am J Respir Crit Care Med 2013; 187:433–438.
35. Campos-Rodriquez F, Martinez-Garcia MA, Reyes-Nuñez N, *et al.* Role of sleep apnea and continuous positive airway pressure therapy in the incidence of stroke or coronary heart disease in women. Am J Respir Crit Care Med 2014; 189:1544–1550.
36. ▪▪ Jauch EC, Saver JL, Adams HP Jr, Bruno A, *et al.* Guidelines for the early management of patients with acute ischemic stroke. Stroke 2013; 44:870–947.

The goal of these guidelines is to limit the morbidity and mortality associated with stroke. The guidelines support the overarching concept of stroke systems of care and detail aspects of stroke care from patient recognition; emergency medical services activation, transport and triage; to the initial hours in the emergency department and stroke unit. The guideline discusses early stroke evaluation and general medical care, as well as ischemic stroke, specific interventions, such as reperfusion strategies, and general physiological optimization for cerebral resuscitation.

37. Su VY, Liu CJ, Wang HK, *et al.* Sleep apnea and risk of pneumonia: a nationwide population-based study. CMAJ 2014; 186:415–421.
38. Gagnadoux F, Le Vaillant M, Goupil F, *et al.* Depressive symptoms before and after long-term CPAP therapy in patients with sleep apnea. Chest 2014; 145:1025–1031.
39. Sharma SK, Agrawal S, Damodaran D, *et al.* CPAP for the metabolic syndrome in patients with obstructive sleep apnea. N Engl J Med 2011; 365:2277–2286.
40. Yaffe K, Laffan AM, Harrison SL, *et al.* Sleep disordered breathing, hypoxia, and risk of mild cognitive impairment and dementia in older women. JAMA 2011; 306:613–619.
41. Nemeth D, Csábi E, Janacsek K, *et al.* Intact implicit probabilistic sequence learning in obstructive sleep apnea. J Sleep Res 2012; 21:396–401.
42. Bucks RS, Olaithe M, Eastwood P. Neurocognitive function in obstructive sleep apnoea: a meta-review. Respirology 2013; 18:61–70.
43. ▪▪ Troussière AC, Monaca Charley C, Salleron J, *et al.* Treatment of sleep apnoea syndrome decreases cognitive decline in patients with Alzheimer's disease. J Neurol Neurosurg Psychiatry 2014; 14:1–4.

In this pilot study, CPAP treatment of severe SAS in mild-to-moderate Alzheimer's disease patients was associated with significantly slower cognitive decline over a 3-year follow-up period. This result emphasizes the importance of detecting and treating SAS in this population.

■麻酔科

進化するビデオ喉頭鏡

気管挿管は気道を確保するために必須の手技である。全身麻酔時の気道確保や人工呼吸器を装着する患者の気道確保，心肺蘇生時の気道確保など，医療現場では気管挿管を実施する機会は多い。

気管挿管の手技は喉頭鏡を用いて実施される。喉頭鏡にはマッキントッシュタイプのものが多く使われているが，声門の確認が容易でない症例に遭遇することも稀ではない。そのような挿管困難症例への対処として，これまでは盲目的に挿管したり，ファイバースコープを用いて挿管したりすることが多かった。

最近ビデオ喉頭鏡が登場し，声門の視認性が向上し気管挿管の安全性が格段に向上している[1]。代表的なビデオ喉頭鏡に，エアウェイスコープ（AWS）®やマックグラス（McGRATH™ MAC）がある。ビデオ喉頭鏡は，喉頭鏡の先端に小型カメラと光源を装着し，口腔内の様子や挿入具合を小さなスクリーンに映し出して画面で観察しながら挿入できるようになっており，カメラを通して間接的に声門を確認できる。気管チューブが声門を通過する様子も視認できるため，食道への挿管も防止できる。

ビデオ喉頭鏡は，挿管困難が予想される患者，肥満患者，口の小さな患者，頸部伸展に制限がある患者，頸髄損傷が疑われる患者などに有用である[2]。しかし，ビデオ喉頭鏡が決して万全というわけではなく，ビデオ喉頭鏡が気管挿管の安全性を保証しているわけではない。

【文献】

1) Mort TC: Crit Care. 2013; 17(6): 1019.
2) Shirgoska B, et al: Acta Clin Croat. 2012; 51(3): 457-61.

【解説】

外 須美夫　九州大学麻酔・蘇生学教授

■加齢医学

認知症診療高齢者の急増

2013年6月に厚生労働省長寿科学研究（朝田班）において，認知症高齢者の心理検査を含む厳密な調査が日本各地のモデル地区で行われ，高齢者の15%，推計462万人が認知症に罹患していることが報告された[1]。軽度認知機能障害（MCI）も14%，推計400万人以上に上ることが明らかとなり，また年齢による有病率は85歳以上で1/3以上，95歳以上では8割以上に上り，長生きをすれば誰もが認知症になるリスクが存在することが明らかとなった。今後，診断困難な例には地域で行える簡易スクリーニング方法（DASC-20）が採用され，ケアプランテキストの整備とともにモデル事業が開始される予定である。

認知症予防の観点からは，幼少時から生涯にわたる知的活動が高い場合，晩年の認知機能低下が遅いという，後方視的縦断病理学的研究が発表されている[2]。これは年齢，性，老人斑，神経原線維変化，ラクナ梗塞，レビー小体で補正した結果であり，同一程度の病理的背景では「知的予備能」を高めることで認知症発症を遅らせることが可能であるという報告である。

認知症の中核症状とBPSDのそれぞれに有効な短期集中リハビリテーション[3]を介入させることで，早期の在宅への退院を促す方向性が，2014年度の診療報酬改定にも盛り込まれた。

【文献】

1) 朝田 隆：臨神経. 2012; 52(11): 962-4.
2) Wilson RS, et al: Neurology. 2013; 81(4): 314-21.
3) Toba K, et al: Geriatr Gerontol Int. 2014; 14(1): 206-11.

【解説】

入谷 敦，*森本茂人　金沢医科大学高齢医学科　*教授

Geriat. Med. 52(4)：353～357, 2014

Seminar

4. サルコペニア，フレイルにおけるビタミンDの意義

大黒　正志　　森本　茂人

KEY WORD　■サルコペニア　■フレイル　■高齢者　■ビタミンD　■低栄養

SUMMARY

■フレイルの定義には栄養障害が含まれる場合が多いが，高齢者に起こりやすい栄養障害は疾病の発症に関与するほか，骨格筋にも影響を与え身体能力にも影響する．フレイルの大きな一因であるサルコペニア自体でも，下肢筋力が低下し，歩行速度の減少，活動量の低下がみられる．フレイルとサルコペニアには重複がみられ，どちらにも低栄養が大きく関わる．加齢に伴い高齢者にはビタミンD不足状態が多く，骨粗鬆症の治療薬としても汎用されるビタミンDは，転倒リスクを減少させることが知られている．また，骨格筋細胞にビタミンD受容体が発現していることが報告されており，ビタミンDのサルコペニアにおける予防と治療の可能性が示唆されている．

はじめに

高齢者の増加に伴い，医療や介護のあり方が問題となってきている．高齢になるに従い徐々に身体機能が低下し，日常生活自立度・活動性が低下し要介護状態となる．フレイルとは，高齢者が抱える普遍的な問題であるが，その概念が出現したのは1980年以降と比較的新しい．フレイルは，Friedらによって表されるように，「加齢に伴って様々な要因が関与して生じ，複数の臓器・器官の機能低下によりストレスに対する脆弱性が増し，有害健康転帰(障害，要長期介護，死亡など)につながる病態」，と理解されている[1]．低栄養，サルコペニア，活力低下・うつはフレイルの主な要因であり，ほかには，骨粗鬆症や視力・聴力の障害など様々な要因が関わる．近年，ビタミンDは栄養面のみならず，転倒・骨折の惹起因子にも深く関わっていることが明らかになり，骨折予防効果をはじめ，様々な老年病疾患に関わるとして注目されるようになった．そこで，本稿ではフレイル，サルコペニアにおけるビタミンDの意義について概説する．

サルコペニアとフレイル

サルコペニアは，1989年にRosenbergによって「加齢による筋肉量減少」を意味する用語として提唱されたが，明確な定義や診断基準がないまま推移してきた．そこで，栄養学と老年医学に取り組む複数の欧州の機関がワーキンググループ(European Working Group on Sarcopenia in Older People：EWGSOP)を組織し，サルコペニアの実用的定義，診断基準，測定手段などを検討した結果を2010年に発表した．これによると，サルコペニアの定義は「身体的な障害や生活の質の低下，および死などの有害な転帰のリスクを伴うものであり，進行性および全身性の骨格筋量および骨格筋力の低下を特徴とする症候群」としている．診断基準は**表1**に

■おおくろ　まさし(金沢医科大学高齢医学准教授)／もりもと　しげと(金沢医科大学高齢医学教授)

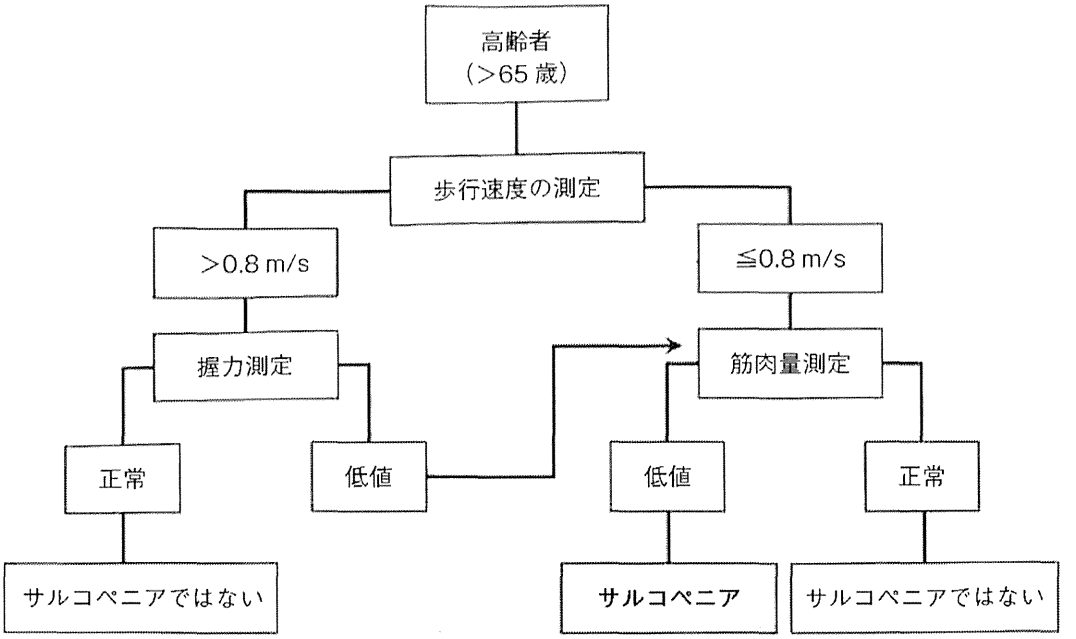

図1　サルコペニア診断のアルゴリズム(文献2より引用)

表1　サルコペニアの診断基準(EWGSOP)

サルコペニアの診断には，基準1)の存在と，基準2)または3)の存在が必要となる．

1)　筋肉量の低下
2)　筋力の低下
3)　身体能力の低下

筋肉量の低下を必須として，筋力低下か身体能力の低下のいずれかがある場合にサルコペニアと診断する(文献2より引用)．

表2　EWGSOPの概念的なサルコペニアの段階

段階	筋肉量	筋力		身体能力
プレサルコペニア	↓			
サルコペニア	↓	↓	または	↓
重症サルコペニア	↓	↓		↓

①筋肉量の減少のみをプレサルコペニア，②筋肉量の減少と筋力の低下あるいは身体能力の低下のいずれかの低下がある場合をサルコペニア，③3つすべての項目を満たす場合を重症サルコペニアとしている(文献2より引用)．

示すように筋肉量の低下を必須として，筋力低下か身体能力の低下のいずれかがある場合にサルコペニアと診断するとしている．また，サルコペニアの病気分類を**表2**に示す．①筋肉量の減少のみをプレサルコペニア，②筋肉量の減少と筋力の低下あるいは身体能力の低下のいずれかの低下がある場合をサルコペニア，③3つすべての項目を満たす場合を重症サルコペニアとしている．状態の重症度を示しており，臨床に役立つものである．EWGSOPは，高齢患者におけるサルコペニアの症例発見のためのアルゴリズムを提唱している(**図1**)．歩行速度を測定し，0.8 m/秒以下であれば，筋肉量が低値であればサルコペニアと診断するとしている[2]．

フレイルとサルコペニアには重複が多い．ほとんどのフレイル高齢者にはサルコペニアがみられ，サルコペニアを有する高齢者もまたフレイルである．**図2**に示すように高齢者は種々の要因で活動量が低下し，食欲低下などによって栄養摂取量が減少しやすいが，それがサルコペニアにつながり，筋量の減少により基礎代謝量が低下するというように，負の連鎖につながる．サルコペニア自体により下肢筋力が低下し，転倒，歩行速度の減少，活動量の低下が誘発される．低栄養がサルコペニアと関連し，フレイルの中核をなしている[3]．さらに一般的なフレイルの概念は，身体的要因のみならず，精神的側

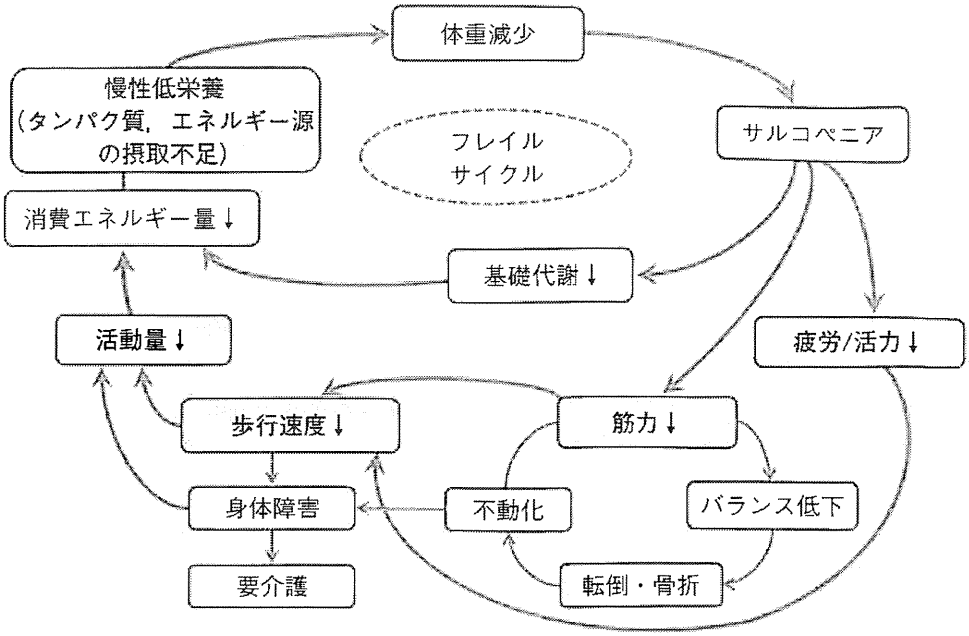

図2　フレイル・サイクル(文献3より引用)

面および認知状態，社会的サポートや環境要因を含んだ社会的側面をも包括している[4]．

ビタミンDの作用

加齢により慢性的にビタミンD摂取量が不足し，また日照射量の減少によって皮膚でのビタミンD産生量が低下すると，血中ビタミンD濃度が低下する．このため，高齢者にはビタミンD不足が多い．ビタミンD不足の影響が最も大きいのが，カルシウム代謝組織である．小腸や腎でのカルシウム吸収能の低下，血中カルシウム濃度の低下，これらに引き続き骨石灰化不全などが起こってくる．さらに，続発的に副甲状腺ホルモン(PTH)の分泌の亢進がもたらされ，骨の再構築のバランスが崩れる．PTH分泌の亢進は骨密度・骨質を低下させ，骨の脆弱化につながる．骨軟化症やくる病患者には，骨脆弱化に加えて筋力低下もみられることから，ビタミンDは筋にも作用し，その不足状態は悪影響を及ぼすことが知られてきた．基礎的研究では，大腿骨頸部骨折例の筋組織において，ビタミンD充足群に比べて欠乏群ではII型筋線維の萎縮が確認されている[5]．また高齢者では，筋組織内のビタミンD受容体量が減少していることも報告されている[6]．

また近年，高齢者や前立腺癌・乳癌・大腸癌・炎症性大腸炎・糖尿病の患者において，血中ビタミンD濃度が低値である場合が多いと報告されており，ビタミンD不足が関わる疾患が究明されてきている[7]．

ビタミンDの効果

Stocktonらの最新のメタ解析によると，17のランダム化比較試験における被験者5,072名を対象とした解析において，血中25(OH)D濃度が25 nmol/Lを超えていた場合には，ビタミンD投与による握力(SMD −0.02，95%信頼区間(CI) −0.15〜0.11)や下肢近位筋力(SMD −0.1，95%信頼区間(CI) −0.01〜0.22)の有意な増加はみられなかった．しかし，血中25(OH)D濃度が25 nmol/L未満であるビタミンD不足の被験者のみを対象とした解析では，ビタミンDの投与により股関節周囲筋力が有意に増加していた(SMD 3.52，95%信頼区間(CI) −2.18〜4.85)．以上の結果から，ビタミンD投与による筋力増強効果は誰にでも生じるというわけではなく，ビタミンD不足の状態にある成人のみに有効であったと報告している[8]．