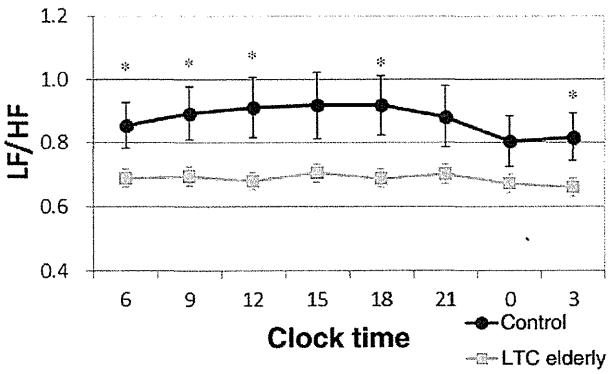

Figure 1 The activity of low frequency/high frequency (LF/HF) in long-term care (LTC) elderly and controls. The RR interval data were measured every 5 min, and averaged every 3 h. $*P < 0.05$, mean ± SEM,

Next, we followed the survival of LTC elderly, and 23 people died among 105 LTC elderly during a mean follow-up period of 8.9 months. The major cause of death was pneumonia ($n = 12$). There was no sign of stroke among the study participants, and one participant with acute myocardial infarction was observed during the follow-up period. Mortality according to HRV indices divided by the average is shown in Table 3. After adjustment for covariates, of all HRV indices, only LF/HF was associated with mortality. Kaplan–Meier survival curves also showed an association between decreased LF/HF and high mortality (Fig. 2). In addition to adjusted covariates, BMI, Barthel Index, and blood nutritional data were not different between the high LF/HF group and low LF/HF group (data not shown).

Discussion

In the present study, we investigated the relationship between physical function, mortality and sympathetic nervous activity measured by HRV in Japanese LTC elderly, and it was shown that LF/HF was significantly decreased in LTC elderly after adjustment for age, sex, CVD risk factors and FIM compared with elderly controls. In addition, the circadian rhythm of LF/HF was lost in LTC elderly, and low LF/HF was associated with overall mortality.

In a previous study, low LF/HF was associated with both frailty and mortality in community-dwelling people of whom one-third were frail elderly,[9] and these associations were consistent with the present data. Additionally, low LF/HF was also shown in LTC elderly, and was independent of physical function.

Elevated heart rate or low SDANN leads to cardiovascular disease and low physical function,[17,18] and the same relationship was also observed in LTC elderly. Furthermore, low albumin and low hemoglobin were observed in the high heart rate group, and limited physical function was observed in LTC elderly. These results are supported by a previous report.[19] So it might be possible to improve the physical function of LTC elderly by maintaining their nutritional state. The high LF/HF group has been reported to show high physical function and muscle mass,[4,20] whereas the present data did not show this association. One of the reasons for this discrepancy is thought to be the effect of aging. Aging generally attenuates LF/HF, and the patients in the present study were older than those in other studies.[9,14] Another reason might be autonomic nervous system disturbance. In particular, the circadian rhythm of LF/HF was impaired in LTC elderly.

Circadian imbalance of LF/HF has been shown in some disorders, such as Parkinson's disease, type 2 diabetes mellitus (T2DM) and ischemic stroke;[21–23] and furthermore, physical activity also influences HRV indices.[24,25] In the present study, LTC elderly with Parkinson's disease were excluded, and CVD risk factors including T2DM were matched between LTC elderly and healthy controls, as stroke and physical activity might affect LF/HF. However, the influence of both conditions on LF/HF is controversial. High physical activity and good posture led to high LF/HF activity,[26] whereas it was also suggested that LF/HF was not affected by physical activity.[13] The effect of LF/HF on stroke is also controversial.[23,27,28] In ischemic stroke patients, LF/HF was higher than healthy controls in some studies,[27,28] whereas another study suggested that LF/HF was lower in patients.[23] So the mechanism of LF/HF circadian rhythm disturbance is not clear, though its recovery might be important to increase physical function in LTC elderly. Other reasons why LF/HF and physical function did not show a correlation in LTC elderly might to be the effects of stroke, insufficient exposure to daylight and posture at daytime. All participants were aged over 75 years in the present study, and there is a possibility that asymptomatic lacunar infarction might be observed. It has also been suggested that lacunar infarction disturbs the autonomic nervous system, leading to a decrease in LF/HF and the related value of the autonomic nervous system, resulting in a disappearance of the correlation between physical activity and LF/HF. In addition, exposure to daylight was known to be one of the most powerful rhythmic regulators in the environment.[29] All participants in the present study spent their time indoors for rehabilitation and care. Furthermore, it is known that the supine position increases HF and decreases LF/HF,[30] and LTC elderly participants who were at rehabilitation units or health service facilities might spend more time in bed compared with outpatient controls, leading to low LF/HF and disappearance of the correlation between LF/HF and physical activity in the present study.

Table 2 Multiple regression analysis of heart rate variability indices with physical function and blood nutritional data after adjusted for age, sex and cardiovascular risk factors

	HR	SDANN	LF	HF	LF/HF
FIM	−0.25*	0.28*	0.19	0.15	−0.08
Barthel Index	−0.27*	0.29*	0.08	0.04	0.00
Body mass index	−0.05	0.05	0.00	−0.08	0.19
Albumin	−0.21*	0.25*	0.05	−0.02	0.11
Hemoglobin	−0.20*	0.27*	0.12	0.12	0.05
Total cholesterol	−0.01	−0.05	−0.13	−0.17	0.03

*$P < 0.05$, analyzed in 105 long-term care elderly. FIM, function independent measure; HF, high frequency; HR, heart rate; LF, low frequency; SDANN, standard deviations of the all NN intervals in all 5-min segments of the entire recording.

Table 3 Proportional hazards regression analysis of the impact of heart rate variability measure on overall mortality

	Hazard ratio†	95% Confidence interval	*P*
Unadjusted			
SDANN (ms)	1.84	0.77–4.38	0.171
LF (ms^2)	1.61	0.59–4.38	0.353
HF (ms^2)	2.14	0.72–6.34	0.169
LF/HF	4.73	1.59–14.06	0.005
Age, sex and cardiovascular risk factors adjusted for association with mortality			
SDANN (ms)	1.53	0.60–3.86	0.372
LF (ms^2)	1.65	0.57–4.78	0.357
HF (ms^2)	2.60	0.82–8.22	0.105
LF/HF	3.37	1.02–11.07	0.046
Age, sex, FIM and cardiovascular risk factors adjusted for association with mortality			
SDANN (ms)	1.19	0.44–3.17	0.736
LF (ms^2)	1.49	0.50–4.41	0.475
HF (ms^2)	2.85	0.83–9.83	0.097
LF/HF	3.61	1.08–12.10	0.038

Based on 23 deaths among 105 participants. Mean values of heart rate variability measure are in Table 1. †Hazard ratio of death rates of participants whose heart rate variability were less than average. FIM, function independent measure; HF, high frequency; HR, heart rate; LF, low frequency; SDANN, standard deviations of the all NN intervals in all 5-min segments of the entire recording.

Recent studies showed that decreased HRV indices including LF, HF and LF/HF were associated with CVD risk factors, and decreased LF was an independent predictor of death in elderly people.[31,32] However, the present findings showed that, of all HRV indices, only LF/HF was associated with mortality. This result is supported by a previous study in which, of HRV indices, LF/HF was associated with both frailty and mortality.[9] The major difference between the present study and other studies is whether or not the participants included frail LTC elderly. All participants were LTC elderly in the present study and WHAS-I, which was reported by Varadhan *et al.* and consisted of one-third frail elderly, whereas in other studies the participants were community-dwelling older adults with intact ADL, and they did not consider physical function.[14,32,33] These results suggest that the significance of LF/HF might differ between LTC elderly and elderly with intact ADL and physical function.

There is a discrepancy in the results derived from studies of LTC elderly and studies of elderly with intact physical function regarding sympathetic nervous activity. Exercise activates the sympathetic nervous system, leading to an increase in blood pressure, muscle blood

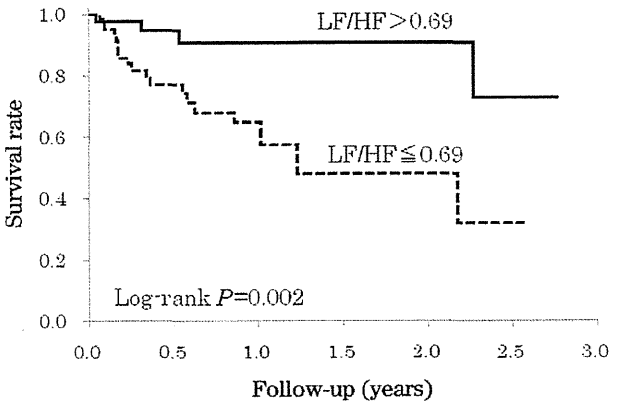

Figure 2 Kaplan–Meyer survival curves for death according to low frequency/high frequency (LF/HF). Mortality was significantly higher for patients with low LF/HF than for patients with high LF/HF. The mean follow-up period was 8.9 months.

flow and muscle strength by inducing muscle protein synthesis,[34–37] suggesting that low sympathetic nervous activity is related to not only physical dysfunction, but also the inability to maintain muscle strength, leading to a worse outcome in LTC elderly. Appropriate activation of the sympathetic nervous system might prevent muscle wasting and improve overall mortality in LTC elderly.

Activation of the sympathetic nervous system has been applied to aging or sarcopenic model rats. The β2-adrenergic agonists, clenbuterol and formoterol, improved muscle mass and muscle strength, and prevented muscle aging in aging, disuse and sarcopenia[38–44] model rats. In contrast, inhibition of sympathetic nervous activity with β-blockers was associated with a worse outcome in older adults.[45] These findings also suggest the importance of preventing a sympathetic nervous activity decline in LTC elderly.

There were several study limitations. First, this was an observational study, and could not provide direct evidence of causality. So it will be necessary to carry out randomized controlled trials to show whether high sympathetic nervous activity leads to a good outcome or not. Second, excessive sympathetic nervous activity is associated with cardiovascular risk factors, such as hypertension, left ventricular myocardial hypertrophy and old cerebrovascular disease.[46,47] In addition, the number of control subjects was relatively small in the present study. Based on these results, it might be hard to apply the findings in the present study to the oldest old population in general. However, some studies, particularly in the elderly, showed that decreased sympathetic nervous activity was associated with a worse outcome.[9] In addition to low physical activity, poor handgrip strength and frailty are known to be important risk factors predicting death older adults,[2,48–50] and few reports have focused on LTC elderly. Therefore, the present study has the possibility of providing evidence to improve physical function and mortality in LTC elderly by means of maintaining or increasing LF/HF.

In summary, the present study showed that LF/HF is a factor that distinguishes LTC elderly from elderly controls independent of physical function. In addition, the circadian rhythm of LF/HF was lost in LTC elderly. Furthermore, low LF/HF was associated with high mortality. For LTC elderly aged 75 years or over, LF/HF might be a predictive biomarker of physical function and mortality.

Disclosure statement

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Chronic lung disease was found to have a strong association with being underweight. It was one of the chronic wasting diseases with systemic inflammation and protein degradation, and the prevalence was higher in the underweight population with greater disease-specific mortality.[9] Sarcopenia was considered the possible pathophysiological mechanism behind the obesity paradox.

The RAP trigger for nutrition was not a good indicator of underweight or obesity. Most MDS items for nutrition were not found to be good indicators of protein or calorie malnutrition.[10] Other tools with better detection sensitivity and specificity, such as bioelectrical impedance analysis for sarcopenia, should be employed in assessment of nutritional risk for nursing home residents.

There are several limitations of this study. First, BMI was not necessarily correlated with measures of body composition, such as visceral adiposity and sarcopenia. Second, the dynamic change in BMI, RAP triggers, and disease diagnosis could not be fully presented in this cohort study. Weight loss, new RAP triggers, and new disease diagnoses were all considered important risk factors for mortality and morbidity. Third, all participants were male, so the results should not be generalized to women.

In conclusion, being underweight was associated with greater risk of mortality after adjustment for age and comorbidities. Chronic lung disease was significantly associated with being underweight. Other than the intervention program for malnutrition, a multidimensional approach for all associated factors would prevent further adverse health outcomes in the elderly population.

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WEIGHT LOSS AND HOMEOSTATIC IMBALANCE OF LEPTIN AND GHRELIN LEVELS IN LEAN OLDER ADULTS

To the Editor: Appetite and food intake decline with age in elderly adults, and their decline results in unintended weight loss, which leads to frailty, morbidity, and mortality.[1] One reason why this anorexic state prevents elderly people from returning to their original weight is impaired regulation of food intake, which makes them likely to be

less hungry and to become rapidly satiated.[2] An imbalance between leptin and ghrelin, two peripheral hormones that signal changes in energy balance to the central nervous system (CNS) and act reciprocally to maintain body weight, may cause predisposition to impaired regulation of food intake.[3]

Sixty-eight elderly adults aged 65 and older (mean age 80.5 ± 5.8 years; female:male ratio 48:20) who were making regular visits to the geriatric outpatient clinic of Kyorin University Hospital were examined. Their diseases were well controlled. Fasting plasma leptin and acylated ghrelin levels were measured using enzyme-linked immunosorbent assay. Because of the potential effects of instrumental activities of daily living (IADLs) on daily energy needs and appetite, they were evaluated by scoring them on the Lawton IADL scale.[4]

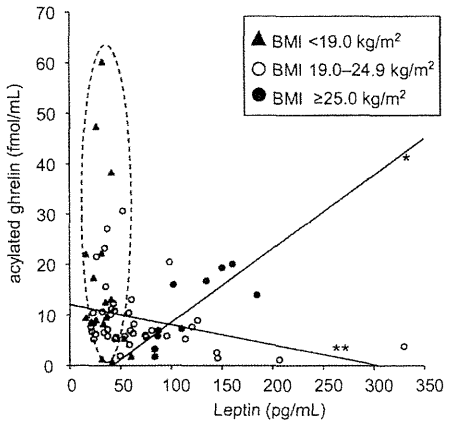
The results of a simple regression analysis showed a positive correlation between subjects' plasma leptin levels and their body mass index (BMI; correlation coefficient (r) = 0.54, P<.001), although there was no correlation between their BMI and ghrelin level (r = −0.23, P = .06), age (r = 0.12, P = .31), or sex (r = 0.08, P = .54). After adjustment for age and sex, the results of multiple regression analysis showed significant correlations between BMI and leptin (partial regression coefficient [prc] = 0.29, P = .02), ghrelin (prc = −0.41, P<.001), leptin–ghrelin interaction (prc = 0.41, P<.001), and IADL scores (prc = 0.26, P = .04). When the subjects were stratified into three groups according to BMI (high, ≥25.0 kg/m^2; normal, 19.0–24.9 kg/m^2; and low, <19.0 kg/m^2), there was a significant positive correlation between leptin and ghrelin levels in the high BMI group (r = 0.79, P = .008) and a significant inverse correlation in the normal BMI group (r = −0.33, P = .03), but no significant correlation was not observed between the two peptides in the low BMI group (r = 0.22, P = .39) (Figure 1).

Leptin is a peptide and the product of the *OB* gene, which is expressed primarily in adipocytes, and it signals the CNS about the quantity of stored fat, whereas ghrelin is an acylated peptide produced in the stomach that relays hunger signals to the CNS. Thus, both peptides mutually act to maintain body weight. The results of the present study confirmed the existence of a strong positive correlation between plasma leptin levels and BMI in elderly adults,[5] as well as a tendency for higher ghrelin levels to be associated with lower BMI,[6] although the results provide preliminary evidence that the feedback control of leptin and ghrelin is limited to a small body weight range.

In the high BMI group, the relationship between the two peptides shifted to a positive correlation with increasing BMI. Regardless of the potential role of leptin in ghrelin regulation, insulin may be an important peripheral peptide in regulating energy balance in obese people. A previous study found that the plasma ghrelin levels of obese subjects depended on whether they had insulin resistance, because the obese insulin-sensitive subjects in their study had higher ghrelin levels, suggesting that compensatory hyperinsulinemia mediated the relationship between obesity and ghrelin.[7] Attenuated postprandial ghrelin suppression in obese subjects may also contribute to impaired satiety signaling and persistent hunger feelings.[8]

The data obtained data in the current study showed that all three subjects with the highest ghrelin levels were in the low BMI group. This is consistent with previous observations that plasma ghrelin levels increase under conditions associated with negative energy balance, such as body weight loss or anorexia, reflecting the ghrelin compensatory response to undernutrition. However, some individuals in the low BMI group had low ghrelin levels, which may reflect aging[9] or atrophic changes in the gastric mucosa, and their low ghrelin levels may have caused delayed gastric emptying that in turn suppressed food intake. A sedentary lifestyle and psychological and social factors may also underlie anorexia in elderly adults because the results of the current study showed that higher IADL scores were associated with higher BMI.

Further study will be needed to determine whether treating lean elderly adults with ghrelin would increased their food intake, although a comprehensive approach to lifestyle factors is now the best conceivable approach to preventing low body weight and sarcopenia in elderly adults.[10]



*r=0.79, p=.008 for BMI ≥25.0 kg/m²
**r=–0.33, p=.03 for BMI 19.0–24.9 kg/m²

Figure 1. Relationship between plasma leptin and acylated ghrelin levels of elderly adults attending a geriatrics clinic according to body mass index (BMI). Solid lines represent the statistically significant linear regressions of the data.

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ARE GERIATRIC SYNDROMES ASSOCIATED WITH RELUCTANCE TO INITIATE ORAL ANTICOAGULATION THERAPY IN ELDERLY ADULTS WITH NONVALVULAR ATRIAL FIBRILLATION?

To the Editor: Age is associated with risk of atrial fibrillation (AF) and its consequences, including stroke. In turn, stroke has been associated with mortality, disability, and health-related quality of life.[1] The American Association of Chest Physicians states that anticoagulation therapy (AT) must be initiated in individuals with nonvalvular AF in moderate- and high-risk categories for the development of stroke (according to congestive heart failure, hypertension, aged ≥75, diabetes mellitus, stroke, vascular disease, aged 65–74, sex (CHA_2DS_2VASc) score),[2,3] whereas a variety of major bleeding prediction scores, such as the hypertension, abnormal (renal/liver function), stroke, bleeding tendency, labile international normalized ratio, elderly, drugs (HAS-BLED) have been developed to aid in the decision-making process in relationship to prescribing AT.[4] Nevertheless, recent work has shown that the net clinical benefit favors the initiation of AT over the risk of major bleeding, even in individuals at high risk of bleeding.[5]

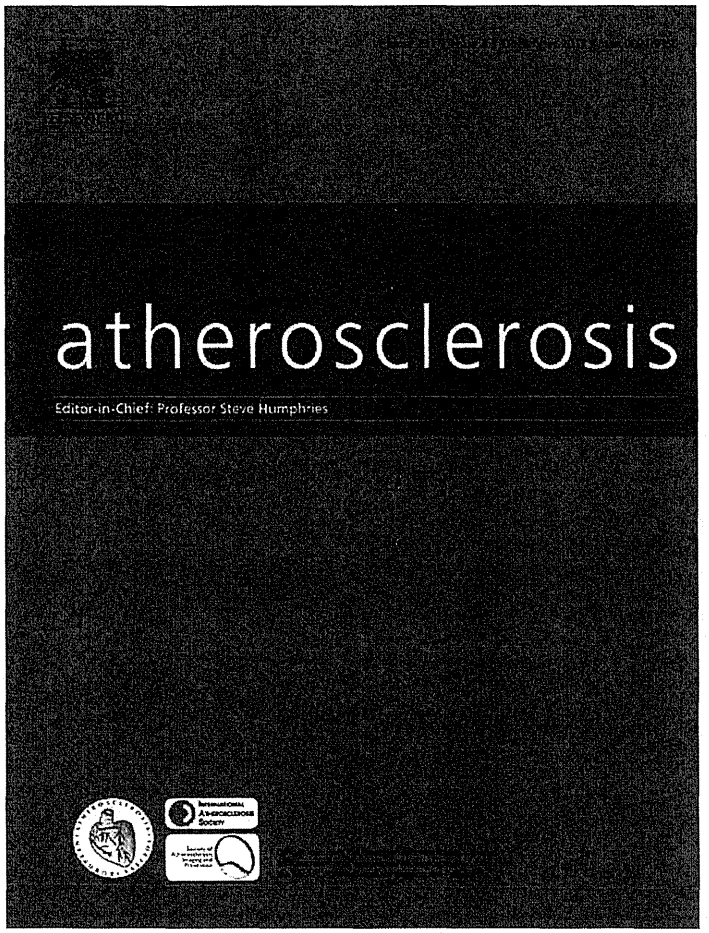
Bleeding risk in elderly adults with AF is frequently overestimated, whereas thrombotic risk is underestimated.[1,6] Thus, AT is underused in this context. It is likely that age-related factors such as functional status, falls, and cognitive impairment influence the decision to anticoagulate these individuals, although an association between the presence of geriatric syndromes (GSs) and the reluctance to initiate AT in elderly adults with nonvalvular

Table 1. Multivariate Logistic Regression of the Absence of Oral Anticoagulation Therapy

	Univariate Analyses, n = 137	Model 1, n = 136	Model 2, n = 129	Model 3, n = 128	Model 4, n = 128
Characteristic	Odds Ratio (95% Confidence Interval)				
Age	1.03 (0.97–1.08)	1.02 (0.96–1.08)	—	1.03 (0.96–1.11)	1.04 (0.96–1.12)
Female	0.70 (0.35–1.37)	0.61 (0.29–1.27)	—	0.55 (0.21–1.42)	0.58 (0.22–1.55)
Lives alone	0.67 (0.20–2.22)	0.82 (0.24–2.82)	—	1.03 (0.23–4.65)	0.94 (0.20–4.35)
Education, years	0.96 (0.90–1.02)	0.94 (0.88–1.01)	—	0.95 (0.88–1.48)	0.97 (0.89–1.06)
Hearing impairment	1.66 (0.84–3.27)	—	1.57 (0.66–3.73)	—	—
Visual impairment	2.09 (0.97–4.53)	—	2.45 (0.89–6.78)	2.84 (0.99–8.16)	—
≥3 falls/years	2.37 (1.01–5.53)[a]	—	1.61 (0.53–4.86)	—	—
IADLs disability	0.64 (0.26–1.56)	—	0.81 (0.26–2.56)	—	—
ADLs disability	0.49 (0.25–0.97)[a]	—	1.43 (0.58–3.55)	—	—
Depressive symptoms	5.12 (2.19–11.99)[b]	—	4.59 (1.73–12.12)[a]	4.94 (1.81–13.52)[a]	5.14 (1.84–14.34)[a]
Cognitive impairment	7.97 (3.62–17.53)[b]	—	7.32 (2.98–17.99)[b]	6.79 (2.73–16.87)[b]	6.27 (2.54–15.46)[b]
CHA_2DS_2VASc stroke risk score	1.03 (0.06–16.80)	—	—	—	1.02 (0.04–22.71)
HAS-BLED	2.58 (1.27–5.23)[a]	—	—	—	2.52 (1.03–6.16)[a]

Model 1 included age, sex, living situation, and educational level; Model 2 included hearing impairment, visual impairment, falls, instrumental activities of daily living (IADLs) and activities of daily living (ADLs) disability, depressive symptoms, and cognitive impairment; Model 3 included age, sex, living situation, educational level, visual impairment, depressive symptoms, and cognitive impairment; Model 4 included depressive symptoms and cognitive impairment and was adjusted for age; sex; living situation; educational level; congestive heart failure, hypertension, aged ≥75, diabetes mellitus, stroke, vascular disease, aged 65–74, sex (CHA_2DS_2VASc) stroke risk score; and hypertension, abnormal (renal/liver function), stroke, bleeding tendency, labile international normalized ratio, elderly, drugs (HAS-BLED) major bleeding risk score. Depressive symptoms = Geriatric Depression Scale (GDS) >5; Cognitive impairment = Mini-Mental State Examination (MMSE) ≤ 23.

$P <$ [a].05, [b].001.



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Efficacy of combined use of three non-invasive atherosclerosis tests to predict vascular events in the elderly; carotid intima-media thickness, flow-mediated dilation of brachial artery and pulse wave velocity

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ABSTRACT

Background: Intima-media thickness (IMT) of the carotid artery, flow-mediated dilation (FMD) of the brachial artery, and pulse wave velocity of the central artery (PWV) have been widely used to evaluate progression of atherosclerosis. Our previous work has revealed that IMT, FMD and PWV are related to each other, and the combination of these measurements was useful in identifying patients with atherosclerotic disease. The aim of the present study was to investigate whether combination of these measurements would predict future cardiovascular events better than each test alone.

Methods and results: From November 2000 to March 2008, 274 consecutive elderly subjects (men/women; 114/160, mean age; 71 ± 12 years) were enrolled in this study. We measured IMT, FMD, and PWV in all of these subjects and followed them for a mean of 41 ± 28 months. During the follow-up period, vascular events occurred in 42 patients (15.3%). IMT (hazard ratio = 1.28 [95%CI, 1.09–1.50], $p = 0.002$ per 0.1 mm increase in mean IMT) and brachial-ankle (ba) PWV (hazard ratio = 1.06 [95%CI, 1.01–1.10], $p = 0.015$ per 1 m/s increase in baPWV) were independent predictors of future vascular events by Cox proportional hazard analysis, although FMD did not reach statistical significance (hazard ratio = 0.85 [95%CI, 0.72–1.01], $p = 0.062$ per 1% increase in %FMD). Importantly, the number of tests showing results in the worst tertile was a more powerful predictor (hazard ratio = 2.21 [95%CI, 1.42–3.43], $p = 0.0004$ for number of tests showing worst tertile) of future vascular events than either IMT, baPWV, or FMD alone. When both IMT and baPWV (with respective cut-off values of 0.98 mm and 19.1 m/s) were taken into consideration, the efficacy increased as compared with each test alone (odds ratio 4.9).

Conclusion: These results indicate that IMT and baPWV, especially when combined, are useful in predicting future vascular events in elderly subjects.

1. Introduction

Recently, noninvasive tests of atherosclerosis have been clinically available, such as common carotid intima-media thickness (IMT), flow-mediated dilation (FMD) of the brachial artery, pulse wave velocity (PWV), beta stiffness index, and systemic arterial stiffness [1]. Several epidemiologic studies have shown that IMT, PWV, and FMD are important, independent determinants of cardiovascular risk in patients with cardiovascular disease [2–5], or diabetes mellitus [6,7] and healthy adults [1,8–12]. These three tests assess different aspects of atherosclerosis; carotid IMT reflects structural changes in the artery wall [13], PWV reflects central arterial stiffness, and FMD reflects endothelial function. While the majority of previous studies utilized a single method to evaluate atherosclerosis, several recent studies showed that combination of two measurements may strengthen the predictive power for future cardiovascular events [14,15].

Consistent with these studies, our previous article showed that a combination of IMT, FMD and PWV was able to predict more reliably the prevalence of atherosclerotic disease in an elderly population than did each test alone [16]. However, it is not clear whether the combination of these three tests is more reliable in predicting future vascular events than is each single test. Thus, the purpose of the present study was to prove the hypothesis that the combination

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of the three different methods to evaluate atherosclerosis would strengthen the predictive power over each test alone. For this purpose, we followed vascular events in patients in whom IMT, FMD and PWV were measured in advance.

2. Methods

2.1. Subject background

From November 2000 to March 2008, 274 consecutive subjects from outpatients of the Department of Geriatric Medicine, Kyorin University Hospital (Tokyo, Japan) were enrolled in this study (Table 1). Three non-invasive atherosclerosis tests (IMT, FMD and PWV) were performed in these subjects for the study purpose. All participants gave written informed consent to the study, which was approved by our institutional ethics committee. The study was performed in compliance with the Helsinki declaration. We included all subjects who agreed to participate in the study, and in whom IMT, FMD and PWV were available.

Diabetes mellitus was defined as fasting glucose of 126 mg/dL or higher, or the use of hypoglycemic medication. Resting blood pressure was measured three times in the seated position, and the average of the second and third readings was recorded. Hypertension was defined as systolic blood pressure >140 mmHg, diastolic blood pressure >90 mmHg, or use of medication prescribed for hypertension. Body mass index was calculated as weight (kg)/height^2 (m^2). Total and high-density lipoprotein (HDL) cholesterol were measured in blood samples obtained after a 12-h fast. Low-density lipoprotein (LDL) cholesterol was estimated by the Friedewald equation. Framingham risk score was determined from age, sex, smoking, blood pressures, diabetes, total cholesterol and HDL cholesterol based on the report by Wilson et al. [11].

Table 1
Clinical characteristics of study subjects.

	Vascular event		
	With (n = 42)	Without (n = 232)	p
Sex (male/female)	24/18	90/142	0.026
Age, y/o	74 ± 12	71 ± 12	0.087
Body mass index (kg/m^2)	23 ± 4	23 ± 3	0.208
Number of risk factors	1.8 ± 1.1	1.6 ± 1.0	0.281
Hypertension, n (%)	31 (74)	126 (54)	0.019
Hyperlipidemia, n (%)	14 (33)	115 (50)	0.052
Diabetes mellitus, n (%)	12 (29)	57 (25)	0.582
Chronic pulmonary disease, n (%)	0 (0)	2 (0.9)	0.546
Kidney disease, n (%)	1 (2.4)	8 (3.4)	0.721
Chronic systemic inflammatory disease, n (%)	0 (0)	2 (0.9)	0.546
Smokers, n (%)			
Never	22 (52)	139 (60)	0.364
Past	17 (41)	69 (30)	–
Current	3 (7)	24 (10)	–
History of stroke, n (%)			
Cerebral infarction	7 (17)	14 (6)	0.295
Brain hemorrhage	0 (0)	3 (1)	–
Cerebral thrombosis	1 (2)	1 (0)	–
Cerebral infarction & hemorrhage	0 (0)	2 (9)	–
Multiple cerebral infarction	0 (0)	7 (3)	–
Transient ischemic attack	1 (2)	0 (0)	–
Unknown	2 (5)	6 (3)	
History of IHD, n (%)			
Angina pectoris	3 (7)	7 (3)	0.560
Myocardial infarction	0 (0)	4 (2)	–
Unknown	0 (0)	3 (1)	–
Atherosclerosis measurements			
Mean IMT, mm	1.06 ± 0.21	0.94 ± 0.19	0.000
FMD, %	2.01 ± 1.71	2.83 ± 2.42	0.045
baPWV, m/s	22.5 ± 6.6	19.7 ± 6.5	0.018
Medication			
ACEI/ARB, n (%)	13 (33)	54 (24)	0.210
Ca blocker, n (%)	14 (35)	58 (16)	0.185
β-Blocker, n (%)	3 (8)	10 (4)	0.383
Statin, n (%)	5 (12)	38 (17)	0.426
Anti-platelet agent, n (%)	15 (38)	42 (19)	0.009

Data are expressed as mean ± SD. FMD, flow-mediated dilation of right brachial artery; IMT, intima-media thickness of common carotid artery; baPWV, brachial-ankle pulse wave velocity, IHD, ischemic heart disease; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; Smoker Never, no smoking history; Smoker Past, previously smoked and quit; Smoker Current, currently regularly smoking.
Student's t test for continuous variables and χ^2 test for categorical variables.

2.2. Participant follow-up and CV events

The occurrence of vascular events was investigated by inquiry to the attending doctor (n = 234), examining the patient's clinical record (n = 9), or inquiry to the patient and/or the family by either telephone (n = 13) or mail (n = 18). The majority of cardiovascular events (n = 243/274) was confirmed as follows: angina and myocardial infarction were confirmed by clinical symptoms and/or coronary arteriography; cerebral hemorrhage, subarachnoid hemorrhage, cerebral infarction and transient ischemic attack were confirmed by clinical symptoms followed by computed tomography, MRI and/or angiography; heart failure, renal failure and arteriosclerosis obliterans were diagnosed according to the clinical guidelines; and aortic dissection was confirmed by contrast computed tomography.

2.3. Measurements of atherosclerosis

Measurements of atherosclerosis were performed as previously described [16]. All examinations were performed by the same skilled technician throughout the study. The subject reclined on the examination table for at least 15 min before the examination to obtain hemodynamic stability.

2.3.1. Measurement of carotid IMT

Common carotid IMT was measured by ultrasound (PowerVision6000, Toshiba) with a 7.5 MHz linear-array transducer. The images were recorded on S-VHS videotape. IMT at the far wall of the common carotid artery was measured by B-mode scan within 10 mm proximal to the bifurcation. Four points were measured in one scan, and mean IMT was calculated [2,16]. The typical error as a coefficient of intra-observer variation in the measurement of IMT was 3.7%, and changes in mean were 2.0%.

2.3.2. Measurement of FMD of brachial artery

The diameter of the artery was measured by ultrasound (PowerVision6000, Toshiba) with a 7.5 MHz linear-array transducer. The images were recorded on S-VHS videotape. The mean diameter of the brachial artery was calculated from four cardiac cycles synchronized with the R-wave peaks on ECG. After a 10 min rest in the supine position, the right brachial artery was scanned. After recording the resting diameter, a cuff was placed around the forearm distal to the target artery and inflated to a pressure of 250 mmHg. Inflation was maintained for 5 min. Maximal vasodilation was observed 45–60 s after cuff release. The change in diameter caused by the restoration of blood flow was expressed as the percent change relative to the initial diameter [16–18]. The typical error as a coefficient of intra-observer variation in the measurement of FMD was 7.4%, and changes in mean were 0.1%.

2.3.3. Measurement of PWV

Brachial-ankle (ba) PWV was measured using an automated device (Form PWV/ABI, OMRON-COLIN, Japan). The average measurement of left and right baPWV was used for analysis. The typical error as a coefficient of intra-observer variation in the measurement of PWV was 2.0%, and changes in mean were 0.2%.

2.4. Statistical analysis

All data are expressed as mean ± SD. Patients were classified according to the tertiles of IMT, %FMD and baPWV. Event rate was calculated using the Kaplan–Meier method, and the statistical significance of differences was investigated by log-rank test. A Cox proportional hazard model was used to determine the variables independently associated with vascular events. Odds ratio was calculated by logistic regression analysis to evaluate the association of event occurrence and each atherosclerosis measurement, with adjusted for age and sex as well as FRS. Receiver operating characteristic curve analysis was performed to estimate the best cut-off point in each test for predicting future vascular events. A p value <0.05 was considered statistically significant.

3. Results

3.1. Subjects

In the 274 patients, the mean duration of follow-up was 41 ± 28 months. During this time, 42 (15.3%) patients experienced vascular events: 14 (33.3%) had angina, 13 (31.0%) stroke, 10 (23.8%) heart failure, 6 (14.3%) renal failure, 3 (7.1%) myocardial infarction, 3 (7.1%) transient ischemic attack, 2 (4.8%) arteriosclerosis obliterans, 2 (4.8%) cerebral hemorrhage, 1 (2.4%) aortic dissection, and 1 (2.4%) subarachnoid hemorrhage.

As shown in Table 1, male sex and hypertension were more frequent in patients with vascular events than in those without events. In addition, patients with vascular events showed thicker mean IMT, smaller %FMD, and greater baPWV than those without events.

3.2. Tertiles and prognostic value of each test

With regard to IMT and baPWV, Kaplan–Meier analysis showed that patients in the worst tertile experienced a higher rate of vascular events than those in the other two tertiles (Fig. 1a, b). A similar trend was also found for %FMD, although not reaching statistical significance ($p = 0.052$ by log-rank test, Fig. 1c). Of note, patients in the three worst tertiles had a markedly higher rate of vascular events than those in the other groups (0, 1, and 2 in Fig. 1d).

In the Cox proportional hazard model, IMT, baPWV, and the number of results in the worst tertiles were significantly associated with vascular events. They remained significant after adjusting for age and sex (Table 2), and FRS (Table 3). FRS alone was not a significant predictive factor ($p = 0.203$, RR 0.987, 95%CI 0.966–1.007).

3.3. Test combination model and vascular events

Receiver operating characteristic curve analysis demonstrated that IMT of 0.98 mm (area under curve = 0.72, sensitivity = 83%, specificity = 57%) and baPWV of 19.1 m/s (area under curve = 0.67, sensitivity = 61%, specificity = 63%) were the best cut-off points for predicting future vascular events.

When the subjects were subdivided into four groups according to the cut-off values of IMT and baPWV, Kaplan–Meier curves showed a stepwise increase in the risk of vascular events (Fig. 2a). Patients with both IMT and baPWV above the cut-off values (group IV) showed the highest rate of vascular events. In addition, the odds ratio of vascular events in group IV was significantly higher than that in group I (Fig. 2b).

4. Discussion

Consistent with the hypothesis, the combination of the three atherosclerosis measurements (IMT, %FMD, and baPWV) was

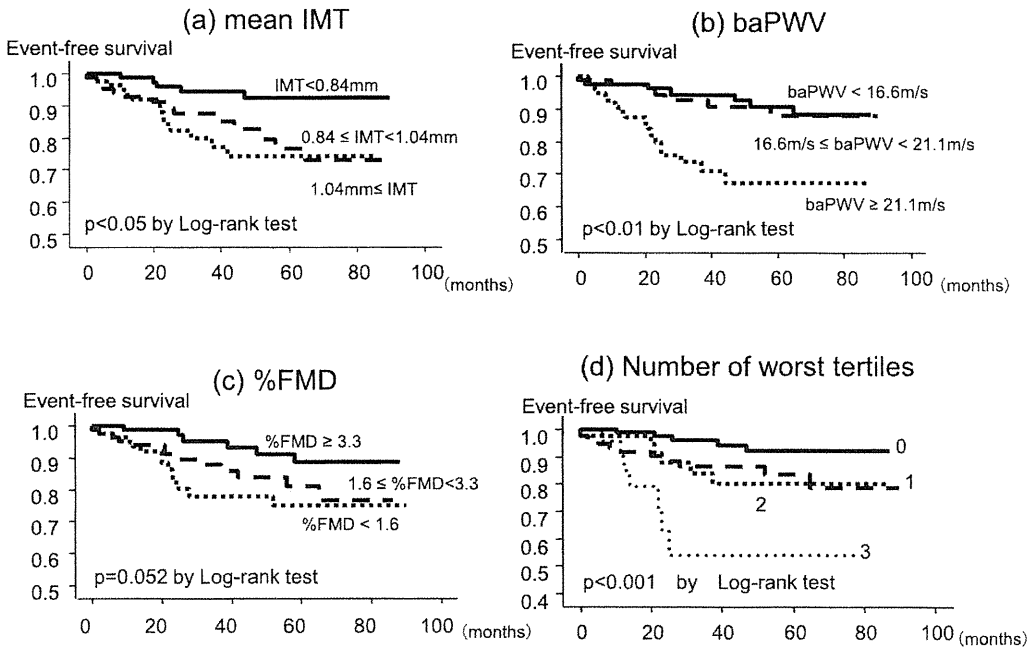

Fig. 1. Kaplan–Meier curves according to tertiles of (a) IMT, (b) baPWV, (c) %FMD, and (d) number of worst tertiles in atherosclerosis tests.

Table 2
Predictive value for future vascular events by Cox proportional hazard analysis adjusted by age and sex.

Variable	Unadjusted ($n = 274$)		Adjusted for age and sex ($n = 274$)	
	HR (95%CI)	p	HR (95%CI)	p
IMT, tertile (increase of 1)	1.836 (1.187–2.840)	0.0064	1.606 (1.002–2.753)	0.0489
IMT, 0.1 mm	1.279 (1.093–1.497)	0.0022	1.226 (1.034–1.454)	0.0191
baPWV, tertile (increase of 1)	2.191 (1.365–3.516)	0.0012	1.969 (1.115–3.476)	0.0195
baPWV, 1.0 m/s	1.055 (1.010–1.101)	0.0152	1.027 (0.970–1.088)	0.3552
FMD, tertile (increase of 1)	1.691 (1.090–2.624)	0.0190	1.631 (0.925–2.342)	0.1029
FMD, 1%	0.849 (0.716–1.008)	0.0615	0.903 (0.756–1.079)	0.2608
Number of worst tertiles	1.930 (1.353–2.754)	0.0003	1.891 (1.229–2.912)	0.0038

HR, hazard ratio; CI, confidence interval; other abbreviations are as in Table 1.

shown to be more powerful in predicting future vascular events as compared with each single test. This finding is consistent with our previous study showing that the combination of these three tests more reliably reflected the prevalence of atherosclerotic disease in the elderly population than did each test alone [16]. Here, IMT, baPWV, and %FMD (although less sensitively) were shown to predict future vascular events in the elderly population. This is in agreement with previous longitudinal studies showing that IMT was a predictor of future vascular disease [2,19], including a study of an elderly population [8], as well as central PWV in a study of subjects over 70 years old [4,11].

With regard to FMD, the present study did not show a significant association with the occurrence of vascular events. Considering the low value and small difference in FMD in the two groups with and without vascular events, one possible explanation for the non-significance is the floor effect. In support of this result, a significant relationship was found between baseline FMD and future cardiovascular events in middle-aged adults [9,10], whereas the prognostic power declined linearly with advancing age from the mid-40s, reaching nearly zero around 70 years of age [20]. Considering the subjects' age in the present study, the non-significance of FMD could be attributable to the advanced age of the patients.

An important point of the present study is that while IMT, baPWV, and %FMD were useful to predict future vascular events, combination of these tests increased the predictive power (Fig. 1d). This finding was consistent with those of our previous cross-sectional study showing that the result of a combination of the three tests was more strongly related to the prevalence of vascular disease in the elderly population than was that of each single test [16]. Several longitudinal studies have shown efficacy of the combination of two different atherosclerosis tests, such as FMD and ankle-brachial pressure index [14], plaque score of the common carotid artery and FMD [15], or carotid IMT and FMD [21], in predicting vascular events. The present study showed strong predictive power of combining three atherosclerosis tests for future vascular events. From our results, it is recommended that three tests should be combined in clinical work to evaluate vascular risk. However, when cost-effectiveness is taken into account, the combination of two tests (IMT and baPWV) would be sufficiently practical for event prediction in the elderly population because FMD requires much more skill and time than does IMT or baPWV. The same idea has been introduced in the recent guidelines from the ACCF/AHA for the assessment of cardiovascular risk in asymptomatic adults [22].

Table 3
Predictive value for future vascular events by Cox proportional hazard analysis adjusted by Framingham Risk Score (FRS).

Variable	Unadjusted ($n = 215$)		Adjusted for FRS ($n = 215$)	
	HR (95%CI)	p	HR (95%CI)	p
IMT, tertile (increase of 1)	1.704 (1.044–2.782)	0.0329	1.669 (1.018–2.735)	0.0422
IMT, 0.1 mm	1.277 (1.069–1.526)	0.0071	1.281 (1.064–1.544)	0.0090
baPWV, tertile (increase of 1)	2.675 (1.522–4.700)	0.0006	2.582 (1.445–4.614)	0.0014
baPWV, 1.0 m/s	1.065 (1.018–1.115)	0.0060	1.060 (1.011–1.111)	0.0166
FMD, tertile (increase of 1)	1.785 (1.072–2.973)	0.0260	1.669 (0.989–2.815)	0.0548
FMD, 1%	0.864 (0.716–1.043)	0.1281	0.888 (0.730–1.080)	0.2339
Number of worst tertiles	2.031 (1.350–3.055)	0.0007	1.991 (1.309–3.027)	0.0013

HR, hazard ratio; CI, confidence interval; other abbreviations are as in Table 1.

Increased carotid IMT has been considered as a marker of subclinical atherosclerosis. Although the biological meaning of IMT remains to be debated, it seems more likely to represent target organ damage related to cardiovascular risk [13]. PWV is the mostly widely used index for evaluating central arterial stiffness. FMD is a tool that is proposed for the assessment of endothelial function and is related to cardiovascular risk, but is not yet a commonly applied method to assess CV risk. Our major finding that the combination of three tests was more predictive than each test alone may be attributable to the fact that each test reflects a different aspect of the progression of atherosclerosis.

The best cutoff value of IMT calculated from event prediction was 0.98 mm in the present study. This value was comparable to previously reported values; approximately ~1.00 mm in healthy adults in spite of populations of different ages; middle age [23–25], over 55 yearsold [26], and 60–74 years old [27]. Although the detailed methodologies were slightly different between studies, ~1.00 mm appears to be relevant to the occurrence of vascular events.

The cutoff value of baPWV calculated from the receiver operating characteristic curve was 19.1 m/s in the present study. This value is slightly higher as compared with values reported previously; that for major cardiovascular events in patients with acute coronary syndrome was 18.0 m/s [28], and that for re-hospitalization and cardiac death in patients with heart failure was 17.5 m/s [29]. On the other hand, the cut-off value for cardiovascular death in community-dwelling elderly people (LILAC study [30]) was higher (25 m/s) than that in the present study. This difference could be explained by the susceptibility to arteriosclerosis in different subjects depending on whether they have preexisting cardiovascular disease and how old they are.

Because of the efficacy of the cut-off values of baPWV and IMT, we investigated the significance of the combination of these two measurements. A stepwise increase in the risk of vascular events was evident by Kaplan–Meier analysis and calculated odds ratio. This is important because much higher predictability can be obtained by simple non-invasive tests. Although FMD did not reach statistical significance, the combination of even three tests would strengthen the predictive power. Indeed, our previous results showed higher prevalence of atherosclerotic disease by combining three tests. Considering the efficacy and simplicity of performance of the three tests, combination of baPWV and IMT (with cut-off values of 19.1 m/s and 0.98 mm, respectively) should be of value for prediction of future occurrence of vascular events in elderly patients.

5. Limitations

One of the limitations of this study was that our approach of three tests for atherosclerosis did not follow the most updated

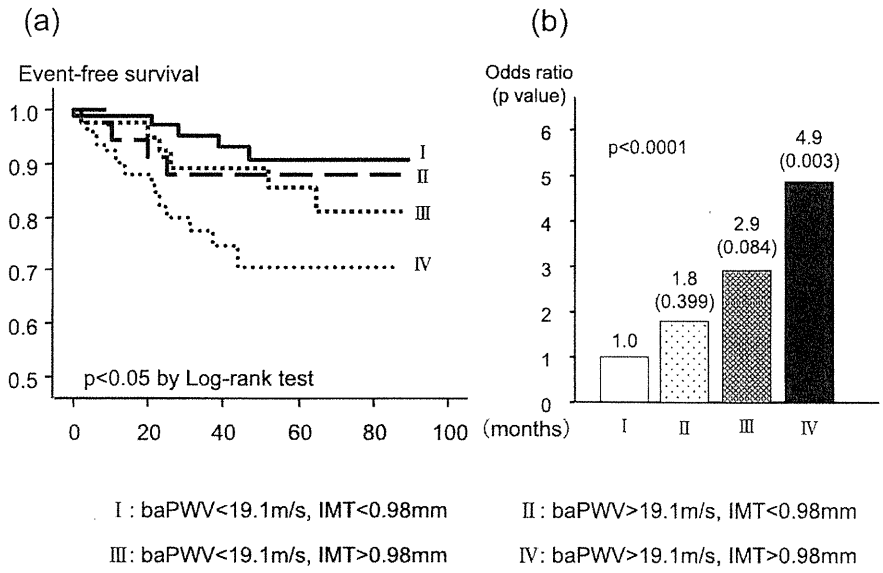

Fig. 2. (a) Kaplan–Meier curves and (b) adjusted relative risks of future vascular events according to cut-off values of baPWV and IMT. Odds ratio and *p* value, in parentheses, are indicated over the bar.

methodologies, because they were not fully established when we started this study. The most recent approaches may provide better predictive values for PWV and IMT, and statistical significance for FMD. Particularly, we manually held the echo probe for FMD measurement, which may have led to low intra-observer reproducibility and no statistical significance.

Second, despite the number of controls, the number of patients was very small.

Third, we included renal failure and heart failure as vascular events since these diseases are thought to be associated with progression of atherosclerosis in the elderly. However, it is possible that heart failure and renal failure may be caused by other etiologies such as collagen disease, infection, valvular disease, etc. Therefore, we also analyzed predictive values excluding heart failure and renal failure as vascular events, and obtained similar results. Thus, the effect of bias in selecting vascular events is considered to be small.

6. Conclusion

IMT, baPWV and, less significantly, FMD, especially when combined, are useful to predict future vascular events in elderly subjects. Because elderly people are at high risk for vascular disease, performing these simple and reliable non-invasive tests will add important clinical information.

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Original Study

Priorities of Health Care Outcomes for the Elderly

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A B S T R A C T

Objectives: Physicians are uncertain about what medical services should be provided to older and/or disabled patients. Better understanding of health outcome prioritization among health care providers and recipients may help the process of decision- and policy-making. For this purpose, surveys were conducted on priorities of health care outcomes for the elderly.
Design: Survey research.
Setting: Four groups of health care providers and four groups of health care recipients.
Participants: A total of 2512 health care providers and 4277 recipients.
Measurements: Questionnaires were sent to more than 8000 health care providers and more than 9000 health care recipients: geriatricians, physicians who commonly see older patients or work in long term care facilities, staff members and participants in adult day care, patients in outpatient geriatric clinics, family members of patients with dementia, and community-dwelling older adults. The questionnaire asked the subjects to rank 12 measures of health care outcomes.
Results: The mean response rate was 49%. All health care provider groups considered "improvement of quality of life" the most important. In contrast, in health care recipient groups, "effective treatment of illness," "improvement of physical function," and "reduction of carer burden" were given high priority, whereas "improvement of quality of life" was perceived as less important. All the groups, including health care providers and recipients, ranked "reduction of mortality" the least important, followed by "avoiding institutional care." Stratification analysis showed that the results did not differ by sex, nursing care level, or the existence of relatives who required nursing care, whereas age slightly influenced the order of high-ranked measures.

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Conclusion: Priorities of health care services and their differences between providers and recipients should be taken into account in the health care of older patients and the design of health care policies and research.

Japanese society has been rapidly aging owing to long life expectancy and a low birth rate.[1] People older than 65 comprised 23.8% of the population in 2012, which is expected to rise to 31.8% in 2030[2] and will be by far the highest in the world. Japanese physicians have been exposed to a high load of older patients, and management of older patients remains a major challenge. There are several reasons for this difficulty. Evidence is still largely lacking for older patients, especially for those older than 75 years, who account for 11.8% of the Japanese population.[2,3] Older patients are likely to have multimorbidities, or co-occurrence of two or more chronic conditions,[4] but application of disease-specific guidelines to older patients with multimorbidities may result in polypharmacy, an increased risk of adverse drug reactions, and poor outcomes.[5,6] At the same time, however, older patients are at increased risk of underuse of necessary medication, for fear of polypharmacy or complications.[7,8]

In an attempt to help optimize prescribing for older patients, investigators have devised numerous tools to guide clinicians, such as lists of indicated, beneficial medication or medication with high potential for harm.[9,10] Although these tools are helpful in reducing exposure of older patients to inappropriate medication and risk of adverse drug events,[11] they do not provide more general considerations, such as when or how to discontinue potentially inappropriate medications, how to balance risks and benefits of unlisted medication, or how to manage medication in special circumstances, such as palliative and hospice care where symptom control is of higher priority. Therefore, the process of determining the medication regimen is inevitably subjective and individualized, taking into account patients' cognitive, physical, and social function, remaining life expectancy, and the goals of care.

Unfortunately, few studies have examined the priorities of health care perceived by health care providers and recipients in geriatric medicine. One small study conducted in England more than 15 years ago showed that geriatricians and patients similarly gave high priority to reducing disability and improving quality of care, and low priority to reducing mortality.[12] However, the serious question of whether there may be a gap in priorities of health care between health care providers and recipients has been raised.[13,14]

Better understanding of health outcome prioritization among health care providers and recipients in geriatric medicine is necessary to help physicians, older patients, and their family members discuss the goals of care and to assist health policy makers in effectively using resources to address the needs of older patients. In this study, we aimed to obtain a comprehensive picture of the views of groups with an important stake in geriatric health care services (geriatricians, physicians who commonly see older patients or work in long term care facilities, staff members and participants in adult day care, patients in outpatient geriatric clinics, family members of patients with dementia, and community-dwelling older adults) on the relative priorities of different outcome measures that are relevant to geriatric clinical practice and health care policy.

Methods

Between September 2010 and October 2011, surveys were conducted in the following eight groups:

(1) All geriatricians (approximately 1500) board certified by the Japan Geriatrics Society
(2) A total of 5000 physicians randomly selected from the list of board-certified physicians in five subspecialties (two internal medicine subspecialties, two surgical subspecialties, and one other) with high exposure to older patients
(3) Physicians working in 800 long term care facilities that were randomly chosen from the nationwide list of long term care facilities
(4) Staff members working in adult day care at 400 randomly chosen long term care facilities as mentioned previously
(5) Participants in adult day care at the same 400 long term care facilities as mentioned previously
(6) Patients in geriatric outpatient clinics at five university teaching hospitals (the University of Tokyo, Kyorin University, Nagoya University, Kyoto University, and Tohoku University)
(7) Family members of patients with dementia who had been seen in geriatric outpatient clinics at four university teaching hospitals (Tohoku University was excluded because of the Tohoku Earthquake at the time of this survey)
(8) A total of 6000 community-dwelling, functionally independent (ie, not requiring nursing care provided by long term care

Table 1
Survey Methods and Number of Valid Answers in 8 Groups

Groups	Time of Survey	Survey Methods	No. of Questionnaires Sent	No. (%) of Valid Answers*
Health care providers				
Geriatricians	2010, Sep	By post	1500	619 (41)
Physicians in 5 subspecialties	2011, Oct	By post	5000	1305 (26)
Physicians in long term care facilities	2011, Oct	By post	800	384 (48)
Adult day care staff	2010, Sep	By post for each facility	400 facilities (2 per facility)	204†
Health care recipients				
Adult day care participants	2010, Sep	By post for each facility	400 facilities (5–10 per facility)	795†
Patients in geriatric outpatient clinics	2010, Sep	Distributed by physicians and returned by post	950	512 (55)
Family members of patients with dementia	2011, Oct	Distributed by physicians and returned by post	542	333 (61)
Community-dwelling older adults	2010, Sep	By post	6000	2637 (44)

*Responses with missing items or invalid answers were excluded.
†For adult day care staff members and participants, questionnaires were sent to each facility by post, where 2 staff members and 5 to 10 participants were offered the questionnaire; 123 facilities (31%) returned the completed questionnaires.

insurance) older adults randomly drawn from the community registers of two target areas (Kashiwa, Chiba Prefecture, a city close to Tokyo, and Sabae, Fukui Prefecture, a provincial city), from which men and women, 65 to 74 years and older than 75 years, were equally selected

Postal questionnaires were sent to all groups of physicians and community-dwelling old adults. For adult day care staff members and participants, questionnaires were sent to each facility, where two staff members and 5 to 10 participants were offered the questionnaire, to be completed on a voluntary basis. The completed questionnaires were gathered at each facility and then returned to us. Patients and family members of patients with dementia received the questionnaires from their physicians (Table 1).

The questionnaire asked about the relative priorities of 12 health care measures that were derived from a literature review and a previous Internet-based survey conducted by the National Center for Geriatrics and Gerontology in 2009 (in Japanese; http://www.ncgg.go.jp/pdf/itaku/21hokoku/20si-3.pdf). Each item was expressed as several words so as to help health care recipients understand the meaning. The respondents were asked to rank the measures in order of priority from 1 (most importance) to 12 (least important). To facilitate ranking the outcomes in order, they were prompted to choose and rank the three most important outcomes, then the three least important outcomes, and last, the six middle outcomes. Ties, or the same ranks, were not allowed.

To examine whether variation in the question wording could affect the results, we devised another version of the questionnaire with different wording for four items and sent that version to a randomly selected subset of participants; however, the results were almost identical (data not shown). We also tested whether the order of health care measures that appeared in the questionnaire would affect the results in a random subset of participants, but the responses to the reverse order questionnaire were similar to those of the original version (data not shown). Therefore, we analyzed the responses from different versions (wording and order) together.

The following information was also collected using the questionnaire: age and sex for all participants; specialty (internal medicine, surgery, psychiatry, or others) and years of experience for physicians; qualification and years of experience for adult day care staff; nursing care level (level of required nursing care: relatively independent, limited impairment, needing extensive help, or severely dependent) for adult day care participants; nursing care level and the existence of relatives who required nursing care for patients in geriatric outpatient clinics; nursing care level, morbid conditions, and the existence of relatives who required nursing care for community-dwelling older adults.

The study protocol was approved by the Ethics Committee of the Graduate School of Medicine, The University of Tokyo. Ethical approval for the surveys on patients in geriatric outpatient clinics and family members of patients with dementia was also obtained from the participating institutions.

Results

The mean response rate for the eight groups was 49%, which varied from 28% for board-certified physicians to 68% for family members of patients with dementia (Table 1). The analytic sample included a total of 2512 health care providers and 4277 recipients.

Tables 2 and 3 show the relative priorities of 12 measures of health care services from the highest importance to the lowest, with mean and 95% CI, perceived by health care providers and recipients, respectively.

All physician groups considered "improvement of quality of life" the most important, and the low mean value for this item across physician

Table 2
Health Care Providers' Priorities for Health Care Outcome

Rank Order	Geriatricians (n = 619)			Physicians from 5 Relevant Subspecialties (n = 1305)			Physicians in Long Term Care Facilities (n = 384)			Adult Day Care Staff (n = 204)		
	Outcome	Mean	95% CI	Outcome	Mean	95% CI	Outcome	Mean	95% CI	Outcome	Mean	95% CI
1	Improvement of quality of life	2.62	2.45–2.80	Improvement of quality of life	3.09	2.96–3.22	Improvement of quality of life	2.88	2.62–3.14	Improvement of quality of life	4.29	3.88–4.71
2	Patient satisfaction with care	4.37	4.15–4.58	Patient satisfaction with care	4.34	4.19–4.49	Patient satisfaction with care	4.60	4.32–4.88	Maintaining a high level of activity	4.35	3.96–4.73
3	Effective treatment of illness	4.80	4.53–5.07	Maintaining a high level of activity	4.64	4.48–4.80	Improvement of physical function	4.68	4.39–4.97	Reduction of carer burden	4.80	4.42–5.17
4	Maintaining a high level of activity	4.92	4.69–5.15	Improvement of physical function	5.25	5.08–5.42	Maintaining a high level of activity	4.73	4.43–5.03	Resolution of assessed problems	5.15	4.74–5.55
5	Improvement of physical function	4.94	4.71–5.18	Effective treatment of illness	5.32	5.13–5.52	Improvement of mental health	5.50	5.29–5.71	Improvement of mental health	5.26	4.86–5.65
6	Improvement of mental health	6.04	5.87–6.20	Reduction of carer burden	5.93	5.79–6.07	Resolution of assessed problems	5.77	5.51–6.04	Patient satisfaction with care	5.43	5.03–5.83
7	Resolution of assessed problems	6.39	6.17–6.61	Resolution of assessed problems	6.12	5.97–6.27	Reduction of carer burden	6.10	5.84–6.37	Improvement of physical function	5.83	5.42–6.25
8	Reduction of carer burden	6.45	6.27–6.64	Improvement of mental health	6.39	6.26–6.52	Effective treatment of illness	6.22	5.87–6.57	Improvement of social functioning	7.17	6.79–7.55
9	Efficient use of resources	7.83	7.67–8.00	Efficient use of resources	7.50	7.37–7.62	Efficient use of resources	8.15	7.95–8.35	Effective treatment of illness	7.41	6.95–7.87
10	Improvement of social functioning	8.80	8.62–8.98	Improvement of social functioning	8.69	8.56–8.82	Improvement of social functioning	8.20	7.95–8.44	Efficient use of resources	7.43	7.04–7.81
11	Avoiding institutional care	10.28	10.15–10.42	Avoiding institutional care	10.24	10.14–10.34	Avoiding institutional care	10.31	10.13–10.50	Avoiding institutional care	9.97	9.71–10.23
12	Reduction of mortality	10.56	10.37–10.76	Reduction of mortality	10.49	10.36–10.62	Reduction of mortality	10.85	10.67–11.04	Reduction of mortality	10.92	10.66–11.17

CI, confidence interval.

Table 3
Health Care Recipients' Priorities for Health Care Outcome

Rank Order	Community-Dwelling Older Adults (n = 2637)			Family Members of Patients With Dementia (n = 333)			Patients in Geriatric Outpatient Clinics (n = 512)			Adult Day Care Participants (n = 795)		
	Outcome	Mean	95% CI	Outcome	Mean	95%CI	Outcome	Mean	95% CI	Outcome	Mean	95% CI
1	Effective treatment of illness	4.23	4.11–4.36	Effective treatment of illness	3.04	2.76–3.32	Effective treatment of illness	2.79	2.58–3.00	Improvement of physical function	3.64	3.42–3.86
2	Reduction of carer burden	4.56	4.44–4.67	Improvement of physical function	4.49	4.19–4.78	Improvement of physical function	4.06	3.84–4.29	Effective treatment of illness	4.33	4.11–4.55
3	Improvement of physical function	5.24	5.13–5.36	Maintaining high level of activity	5.11	4.76–5.45	Improvement of quality of life	5.46	5.19–5.73	Reduction of carer burden	5.40	5.18–5.63
4	Maintaining high level of activity	5.88	5.76–5.99	Reduction of carer burden	5.29	4.98–5.61	Reduction of carer burden	5.52	5.28–5.77	Improvement of quality of life	6.08	5.86–6.30
5	Resolution of assessed problems	5.91	5.76–6.05	Improvement of mental health	5.53	5.24–5.82	Improvement of mental health	5.81	5.58–6.04	Maintaining high level of activity	6.12	5.88–6.37
6	Improvement of mental health	6.26	6.15–6.36	Improvement of quality of life	5.80	5.48–6.13	Maintaining high level of activity	5.97	5.66–6.28	Improvement of mental health	6.38	6.17–6.58
7	Improvement of quality of life	6.36	6.23–6.49	Resolution of assessed problems	5.98	5.69–6.27	Resolution of assessed problems	6.17	5.93–6.42	Patient satisfaction with care	6.44	6.24–6.64
8	Patient satisfaction with care	6.81	6.70–6.92	Patient satisfaction with care	6.01	5.70–6.31	Patient satisfaction with care	6.72	6.47–6.96	Resolution of assessed problems	6.45	6.26–6.65
9	Efficient use of resources	6.91	6.81–7.02	Efficient use of resources	7.49	7.21–7.76	Efficient use of resources	7.46	7.24–7.69	Efficient use of resources	6.57	6.36–6.77
10	Improvement of social functioning	7.44	7.32–7.56	Improvement of social functioning	9.17	8.90–9.45	Improvement of social functioning	8.42	8.18–8.65	Improvement of social functioning	8.22	8.03–8.42
11	Avoiding institutional care	8.43	8.31–8.56	Avoiding institutional care	9.86	9.60–10.12	Avoiding institutional care	9.39	9.16–9.62	Avoiding institutional care	8.61	8.41–8.81
12	Reduction of mortality	9.98	9.87–10.08	Reduction of mortality	10.23	9.99–10.48	Reduction of mortality	10.22	10.00–10.44	Reduction of mortality	9.75	9.55–9.95

CI, confidence interval.

groups indicated physicians' strong preference for this item. All the physician groups also considered "patient satisfaction," "maintaining a high level of activity," and "improvement of physical function" important after "improvement of quality of life," with some variation in the order of their preferences. Geriatricians ranked "effective treatment of illness" the third most important, in contrast to the other two physician groups that ranked this item lower. Adult day care staff ranked "improvement of quality of life" and "maintaining a high level of activity" first and second, respectively, but placed "reduction of carer burden" the third most important, unlike physicians.

With regard to the receiving side of health care, "effective treatment of illness," "improvement of physical function," and "reduction of carer burden" were given high priority, whereas "improvement of quality of life" tended to be perceived as less important.

All the groups, including both health care providers and recipients, ranked "reduction of mortality" the least important, followed by "avoiding institutional care," "improvement of social functioning," and "efficient use of resources," except for the adult day care staff who ranked "improvement of social functioning" higher than "effective treatment of illness."

Stratification analysis demonstrated that the results from physicians were not influenced by sex (male vs female, data not shown); however, physicians older than 60 years tended to rank "effective treatment of illness" and "improvement of physical function" higher compared with younger physicians, who appeared to prioritize "patient satisfaction" and "maintaining a high level of activity." Physicians with more than 30 years' experience, most of whom were older than 60 years, showed a similar tendency, prioritizing "effective treatment of illness" and "improvement of physical function." The results from adult day care staff were identical across groups stratified by age, years of experience, and qualification (data not shown).

The results from the health care recipients did not differ by nursing care level (relatively independent vs limited impairment or higher, or limited impairment vs needing extensive help or higher) for adult day care participants and patients in geriatric outpatient clinics, the existence of relatives who required nursing care (present vs absent) for patients in geriatric outpatient clinics, study site for patients in geriatric outpatient clinics and community-dwelling older adults, or sex for all health care recipient groups (data not shown). Although stratification by age showed that the three measures given highest priority were the same across the age groups (65 to 74 vs older than 75) in community-dwelling older adults, the younger group ranked "reduction of carer burden" first, whereas the older group ranked "effective treatment of illness" first (data not shown).

Discussion

This study is, to our knowledge, the largest survey ever conducted to describe health outcome prioritization in geriatric medicine. We aimed to obtain a comprehensive picture of the views of those involved in decision-making processes in geriatric medicine and compare views between health care providers and recipients. We chose four groups each from providers and recipients that are considered relevant to our purpose. The mean response rate was close to 50%, which was good for a large-scale postal survey and ensured the representative nature of our respondents.

This survey demonstrated that there may be an important gap in health outcome prioritization between health care providers and recipients in geriatric medicine. All health care provider groups, notably physicians, expressed a strong preference for improvement in quality of life (QOL) as a priority of care, whereas health care recipients gave the highest priority to effective treatment of diseases and tended to put lower importance on QOL. In the context of clinical medicine, QOL is often used as a nonspecific, all-encompassing term to describe

nonmortality outcomes averaged over multiple domains (ie, physical, social, and psychological functioning and well-being). Consideration of QOL is essential for the selection of a treatment option, particularly when conditions are noncurative and chronic.[15] Therefore, it is not surprising that physicians who regularly see older patients with multiple chronic conditions consider QOL the most important health care outcome. On the other hand, the term QOL may not be familiar to many health care recipients, and we cannot exclude the possibility that QOL might be confused with other terms, such as standard of living.

Most health care recipients ranked effective treatment of diseases as the most important, suggesting that patients are concerned about their own particular symptoms rather than nonspecific QOL, arguing for efforts to examine the symptoms most concerning to patients. The high importance of effective treatment of diseases ascribed by health care recipients, but not physicians, also implies the significance of the often-neglected aspect of inappropriate prescribing in older adults: underuse of medication likely to be beneficial to older adults. Increased evidence has suggested that failure to prescribe indicated, beneficial medication is common in older adults,[7,8,16] and recent attempts to provide an explicit list of appropriate, indicated medication for older adults are justified.[10]

Interestingly, views on patient satisfaction were also different. All physician groups ranked patient satisfaction as the second top priority, whereas health care recipients considered this to be less important. This tendency has been demonstrated in a prior small study in England more than 15 years ago.[12] Recently, patient satisfaction has been increasingly used to measure health care qualities and compare health plans or physicians.[17] However, our finding may argue against the value of patient satisfaction as a performance measure in geriatric medicine, especially in light of recent evidence suggesting that higher patient satisfaction is accomplished at the sacrifice of increased use of health care resources and may not be directly associated with technical quality of care or improved outcome.[17,18]

We observed agreement on several items between health care providers and recipients. The importance of physical and mental function, such as maintaining activity or improving physical function, was expressed by both health care providers and recipients. This finding was consistent with prior studies in older adults with multiple chronic conditions[12,19] or terminal conditions,[20,21] suggesting that physical and mental function should be an essential factor to consider as a health care outcome in various care settings for older patients.

Reduction in mortality was given the lowest priority by all the groups in health care providers and recipients alike. This view is similar to that observed in previous studies.[12,19] This finding supports the contention that treatment interventions should be assessed in terms of reduced morbidity and improved QOL in addition to reduced mortality.

In this survey, respondents' characteristics, except age, had limited influence on their views on health outcome prioritization within each group. Geriatricians older than 60 years and community-dwelling adults older than 75 years gave higher priority to effective treatment of diseases compared with their younger counterparts. This suggests that health outcome priorities may not be stable, and can change as respondents age or differ from generation to generation. The cross-sectional design of our survey prevented us from separating the age effect from the secular trend, and further studies will be required to examine the time- or setting-dependent variability of health outcome prioritization.

This study has several limitations. First, although the average response rate was high for a postal survey, it was lower in physician groups than in health care recipient groups (26% to 48% vs 44% to 61%, Table 1). Thus, selection bias cannot be excluded. Second, it was not sure that health care recipients, particularly adult day care participants, correctly understood the study terminology. Third, some of the items used in the survey were not mutually exclusive. Nevertheless, a similar trend in priorities of outcome measures according to either side of health care providers or recipients suggests that the overall results were not significantly affected by these limitations.

Conclusion

We demonstrated that there was significant agreement and disagreement of health outcome prioritization between health care providers and recipients in geriatric medicine. Health care providers and recipients agreed on high priority for function and low priority for reduction in mortality, but there was obvious disagreement in how they perceived QOL, treatment effect, and patient satisfaction as goals of care. Such disagreement necessitates better communication between providers and recipients to reach goals of care that are mutually understandable and tailored to meet patients' specific needs. The low importance of reduction in mortality and patient satisfaction ascribed by health care recipients may question the value of these outcomes as a way to assess treatment interventions and quality of care. We propose that the priorities of health care outcomes and their differences between providers and recipients demonstrated in this study should be taken into account in the health care of older patients and the design of health care policies and research.

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