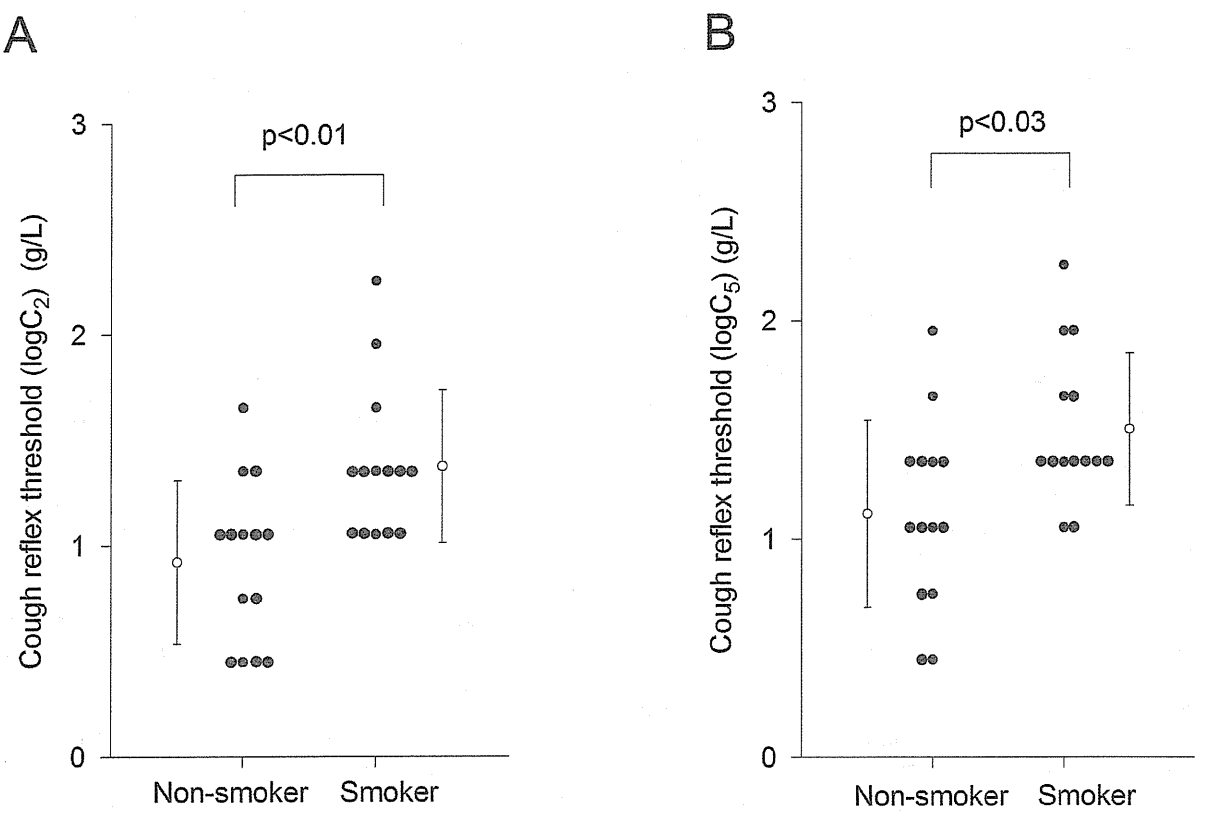

Figure 1 Comparisons of cough reflex sensitivity between non-smokers and smokers. (A) Cough reflex sensitivities are expressed as the log transformation of the lowest concentration of citric acid that elicited two or more coughs (C_2). (B) Cough reflex sensitivities are expressed as the log transformation of the lowest concentration of citric acid that elicited five or more coughs (C_5). Open circles and error bars indicate the mean value and the standard deviation in each group, respectively.

Although cough is usually referred to as a reflex controlled from the brainstem, cough can be also controlled via the higher cortical center and be related to cortical modulations [30]. Therefore, the depression of cough reflex could be due to the disruption of both the cortical facilitatory pathway for cough and the medullary reflex pathway. Since the urge-to-cough is a brain component of the cough motivation-to-action system, the depressed urge-to-cough suggests impairment of supramedullary pathways of cough reflex [6].

It is reasonable to suppose that urge-to-cough arises from sensors that mediate cough reflex. In the bronchopulmonary system, there are at least five sensors involved in this reflex [12]. The dyspnea sensation induced by external resistive loads is reported to be described as the work/effort sensation of dyspnea [31-33]. The neural pathways proposed for this sensation include corollary discharge from motor cortical centers that drive voluntary breathing, and muscle mechanoreceptors and metaboreceptors [33]. Although tobacco smoke may induce desensitization of bronchopulmonary sensors or structural changes interfering with accessibility to sensors [34,35], it is less possible to affect muscle mechanoreceptors and metaboreceptors in healthy young smokers. Therefore, the differential susceptibility to tobacco smoke in peripheral receptors/sensors may explain the dissociation of perceptions of the urge-to-cough by citric acid and dyspnea during external resistive loads. However, in the present study, although cough reflex sensitivity and the urge-to-cough log-log slope were decreased in smokers, the urge-to-cough thresholds did not change (Figure 2). This may suggest no significant changes in bronchopulmonary sensors involved in the urge-to-cough induction and the larger contribution of central gain mechanisms rather than the peripheral ones.

Davenport et al. showed that nicotine administration inhibited urge-to-cough rating scores in smokers deprived from smoking for more than 12 hours [36]. In this study, smokers who withdrew from tobacco smoke showed a greater number of coughs, higher urge-to-cough rating and higher anxiety scores than non-

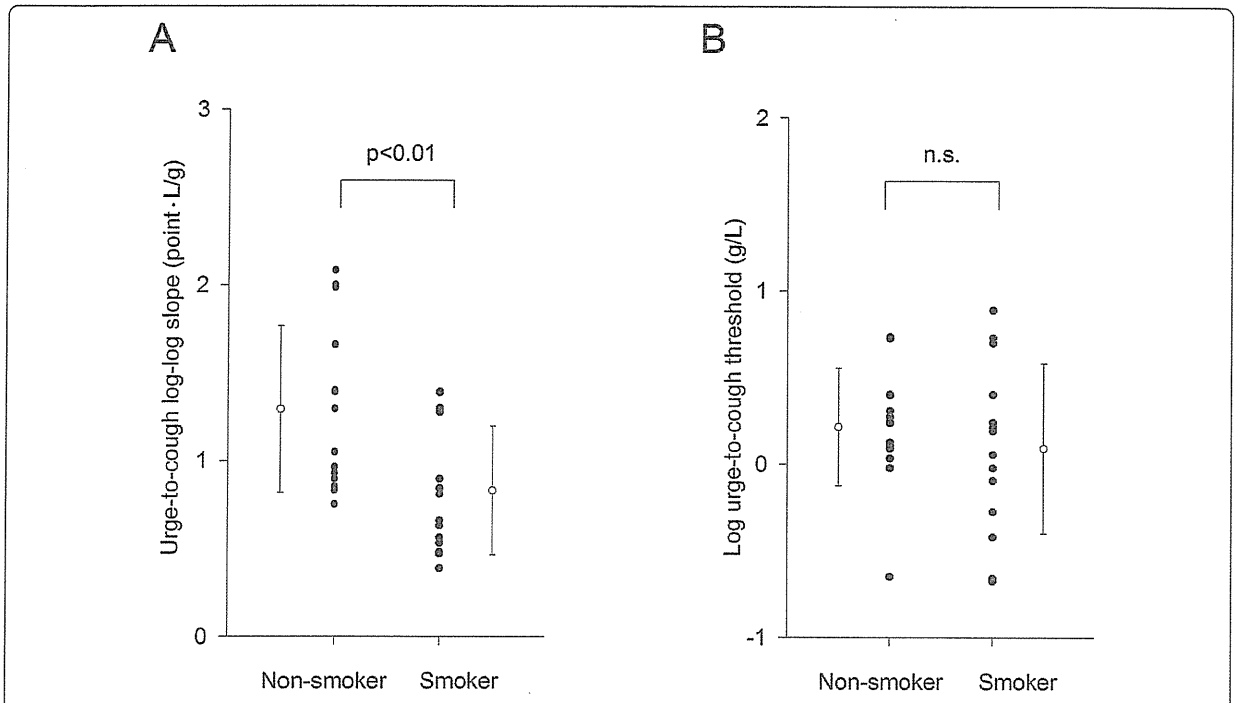

Figure 2 Comparisons of and the urge-to-cough between non-smokers and smokers. (A) The urge-to-cough log-log slope by linear regression between log citric acid concentration and the log Borg scores. (B) The urge-to-cough threshold estimated by log citric acid concentration at the log Borg Score of urge-to-cough = 0. Closed circles indicate the value of each subject. Open circles and error bars indicate the mean value and the standard deviation in each group, respectively. n.s. denotes not significant.

smokers, and the nicotine administration reduced those to match the non-smokers. The study clearly showed the role of nicotine on the central modulation of cough cognitive motivational system and motor response. However, due to a lack of the data concerning smokers without withdrawal from tobacco smoke, the state of cough cognitive motivational system in smokers with depressed cough reflex sensitivity has not been elucidated.

In the present study, we showed the cough cognitive motivational system was inhibited in smokers with depressed cough reflex sensitivity. Since it was reported that nicotine and tobacco smoking induce the endogenous opioid system [37], cognition of the urge-to-cough might be inhibited by endogenous opioids in smokers. However, this is unlikely because we failed to detect the depressed perception of dyspnea which is also inhibited by endogenous opioids [38]. To our knowledge, the depressed perception of dyspnea has not been reported in healthy smokers.

Table 2 Comparison of perceptions of dyspnea between non-smokers and smokers

	Non-smokers	Smokers	P- value
Number	14	14	
R = 10 (point)	2.3 ± 1.0	1.9 ± 1.3	n.s.
R = 20 (point)	3.1 ± 1.4	2.9 ± 1.5	n.s.
R = 30 (point)	4.4 ± 1.5	4.8 ± 1.8	n.s.
Sum (point)	9.7 ± 3.8	9.8 ± 4.8	n.s.
Slope (point • L/g)	0.14 ± 0.05	0.15 ± 0.05	n.s

Data are mean ± S.D. R = 10, R = 20 and R = 30 indicates the Borg score at R = 10, R = 20 and R = 30 $cmH_2O/L/s$, respectively. Sum indicates the summation of Borg scores at R = 10, R = 20 and R = 30 $cmH_2O/L/s$. Slope indicates the linear regression slope when estimated Borg scores were plotted against the corresponding values of resistive loads. P-values were calculated by the Mann-Whitney *U* test. n.s. denotes not significant.

Respiratory sensation such as various types of dyspnea and the urge-to-cough are the result of sensory activation of subcortical and cortical neural pathways. Some of these pathways are shared across respiratory modalities while activation of some neural areas are modality specific [15]. There are many brain imaging studies concerning dyspnea using different techniques to induce dyspnea. Despite the use of different intervention techniques, the common predominant neural activity has been found in the insula, operculum, and frontal cortex areas, the anterior cingulated cortex, the posterior cingulated cortex, the cerebellum, the thalamus, and the amygdala [13,39]. In contrast, there is only one brain imaging study concerning the urge-to-cough by Mazonne et al. [14]. Their functional magnetic resonance imaging study showed activation in insula,

anterior cingulated, primary sensory cortex, orbitofrontal cortex, supplementary motor area and cerebellum during the induction of the urge-to-cough by capsaicin [14]. Although it is still unclear how these brain regions relate to the respiratory sensations, our study may suggest that shared brain regions, such as insula, anterior cingulated, and cerebellum, which are activated by both dyspnea and urge-to-cough are not suppressed by tobacco smoke. Since it has been proposed that initiation of a reflex cough response requires the urge-to-cough to facilitate it [6], the depressed cough reflex sensitivity in healthy smokers might be explained solely by the supramedually mechanism.

Cigarette smoking appears to be a major risk factor for respiratory tract infections [4]. As cough is a normal reflex and respiratory defense mechanism, blunted cough reflex sensitivity may contribute to the risk of respiratory tract infection in cigarette smokers. Moreover, since dyspnea is usually a symptom at a relatively advanced stage of respiratory tract infection whereas cough represents at earlier stages, the blunted urge-to-cough may contribute to the development of respiratory tract infections in smokers due to failure to seek proper medical service.

Conclusions

Our study showed that decreased cough reflex sensitivity in healthy smokers was accompanied by a decreased cognition of the urge-to-cough whereas it was not accompanied by the alternation of perception of dyspnea. Physicians should pay attention to the perceptual alterations of cough in smokers.

Abbreviations

C_2: the lowest concentration of citric acid that elicited two or more coughs; C_5: the lowest concentration of citric acid that elicited five or more coughs.

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Authors' contributions

MK and SE participated in the design of the study, collected and analyzed data, and drafted the manuscript. EN, PG, CS and MY participated in the design of the study and collected the data. TE and MK participated in design of the study and helped to draft the manuscript. All the authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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ORIGINAL ARTICLE: SOCIAL RESEARCH, PLANNING AND PRACTICE

Understanding the oldest old in northern Japan: An overview of the functional ability and characteristics of centenarians

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Aim: To increase knowledge of the functional ability of centenarians by examining the situation of Japanese centenarians residing in an urban region in northern Japan.

Methods: Questionnaires focused on functional ability, demographics, housing and care needs were received from 56 centenarians and 104 control subjects: 56 aged 80–89 and 48 aged 90–99.

Results: Centenarian physical capabilities, care needs and health history were diversified. Centenarians most commonly resided with family in the community and were likely to utilize informal and insurance care services. Gender differences in functional ability by age groups known as gender cross-over were observed in control subjects but reduced in centenarians. A few who reported physical limitations were not entitled to receive nationally subsidized care services suggesting inaccuracies may have occurred during certification determination.

Conclusion: Centenarians in northern Japan represent a heterogeneous cohort suggesting multiple paths to the attainment of advanced old age. This is the first study designed to provide a solid knowledge base of actual circumstances experienced by centenarians specifically in northern Japan. **Geriatr Gerontol Int 2010; 10: 78–84.**

Keywords: aged, aging, health services for the aged, health status, gender characteristics.

Introduction

Japan, a nation famous for longevity, is one of the fastest graying nations in the world. The Japanese population aged over 65 will rise from 20.1% in 2006 to 26% by 2015 and 30.9% by 2030.[1] The number of centenarians in Japan in 2005 was 25 554, 85.2% being female, and is projected to increase to over 166 000 by 2025.[1] With continuous developments in medical care, people are expected to live longer while the prevalence of individuals living with disabilities and or diseases requiring care is also anticipated to increase.

Due to the historical stigma towards institutionalized care combined with the lack of adequate long-term care facilities, many elderly people were hospitalized for long periods of time in regular hospitals.[2] Long-Term Care Insurance (LTCI) introduced in Japan in April 2000 aimed to increase home care services, reduce the number of hospitalizations and unnecessary medical expenses, and increase support to the elderly and their burdened caregivers.

Centenarians represent a heterogeneous cohort and require a diverse range of care from informal and formal care services. By understanding the strengths and weaknesses of LTCI and its utilization by centenarians in

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Japan, other nations may be able to more effectively customize health-care systems to meet the needs of the oldest old.

This paper aims to provide an analysis of centenarians focusing upon functional ability, social situation, and care status. The authors wished to elucidate the effectiveness of the current LTCI system in allocating care and services to the oldest old.

Methods

This is the first study to investigate centenarians in Sendai City, northern Japan. Sendai City reported 1.4 centenarians per 10 000 people,[3] double the general rate in the USA of 0.7 per 10 000.[4] At the time of this study, the sex ratio of centenarians in Sendai City was 6.75 females to one male.

Resident registrars in Sendai City, the second largest city in northern Japan with a population of approximately 1 million people, were manually searched by the principal investigator (S. F.) and all names, addresses, gender and birthdates of the 135 registered centenarians (individuals aged 100 years or older as of 1 January 2007) were selected for the present study. Simultaneously, 135 people aged 90–99 years and 135 people aged 80–89 years were recorded as controls subjects. Immediately following each centenarian located in the registrar book, the next 80–89-year-old and 90–99-year-old individuals listed in the subsequent pages were selected as control subjects. Of the 405 questionnaires, 160 (39.5%) were completed by 56, 48 and 56 respondents aged 80–89, 90–99 and 100–107 years, respectively, and included for analysis in this study.

Questionnaires mailed on the same date included questions relating to the respondents demographics, activities of daily living (ADL) and instrumental activities of daily living (IADL) levels, and care situation.

Questionnaire respondents were assessed for problems in carrying out ADL using the Barthel Index (BI), a widely used 10-item ADL scale.[5] Individuals were divided into six groups according to BI score based upon research by Gondo:[6] Independent A (score 100); Independent B (score 80–99); Minimal Help (score 60–79); Partially Dependent (score 40–59); Very Dependent (20–39); and Totally Dependent (score <20). Independent (combination of Independent A and B scores) and Dependent (combination of Very Dependent and Totally Dependent scores) were used for analysis.

More complex IADL were evaluated using the IADL scale created by Lawton and Brody.[7] This scale ranges 0–8 points for women and 0–5 points for men where a score of 8 for women or 5 for men means that no help is needed.

To analyze the levels of care required, the LTCI care needs level designations given to recipients by the Japanese Ministry of Health, Labor and Welfare were used. Applicants are categorized into one of three categories: self-supporting, support needs levels 1 through 2 (called "yoshien" in Japanese), or care needs levels 1 through 5 (called "yokaigo" in Japanese). Self-supporting individuals are ineligible to receive LTCI assistance. Support needs levels and care needs levels receive eligibility ranging from the fewest amount of community-based services: Support 1, to the maximum allotted amount of care including community as well as institutional services (Care 5). Individuals with LTCI certification choose which services they receive and the company to provide the care.

Care services used by respondents were divided into informal services provided by unpaid family members and formal services comprised of LTCI services and privately paid services.

Informed consent was obtained from all participants. This study was conducted in accordance with the ethical guidelines of Tohoku University School of Medicine.

Statistical analysis was conducted using Microsoft Office Excel 2003 and SPSS ver. 15.0. Analysis was performed using independent samples tests, two-tailed Student's *t*-test for equality of means, Kruskal–Wallis one-way ANOVA, and test of means using ANOVA. $P < 0.05$ was considered significant.

Results

The status of centenarian and control subjects is shown in Table 1. Fifty-six centenarians ranging in age from 100–107 years (mean 102.0 ± 1.3 years; males : females, 10:46) and 104 control subjects including 56 respondents aged 80–89 (mean 83.7 ± 2.2 years) and 48 respondents aged 90–99 (mean 92.4 ± 2.2 years) were included in this study. No significant differences in response rate were observed between gender or age groups (Fig. 1).

Centenarian physical functioning was lower than 80–99-year-old control subjects ($P < 0.001$). Mean BI scores for 90–99-year-old males were higher than 90–99-year-old females ($P < 0.0001$). There were more Independent centenarian males than females (45.5% vs 18.2%). The percentages of 90–99-year-old and centenarian Independent males were both three times larger than females. The prevalence of Dependent centenarians was 20% more than controls. The proportion of Dependent males was higher than females for both 80–89-year-old (14.82% vs 8%) and centenarian (54.6% vs 47.7%) respondents.

IADL scores showed a general decline as respondent age increased ($P < 0.001$). Differing patterns of IADL status by age were shown between males and females. Males aged 90–99 years showed higher IADL levels than both 80–89-year-old and centenarian respondents.

Respondents reported experiencing various comorbidities including hypertension, dementia, swallowing

Table 1 Background characteristics of participants by age

	80–89 years old			90–99 years old			≥100 years old		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
Characteristics									
No. of participants (%)	56[††]	28 (50.0)	28 (50.0)	48[††]	12 (25.0)	36 (75.0)	56[††]	10 (19.6)	46 (80.4)
Age, mean ± SD	83.7 ± 2.2	83.3 ± 2.0	84.1 ± 2.4	92.4 ± 2.2	92.6 ± 2.4	92.3 ± 2.2	102.0 ± 1.3	101.7 ± 1.3	102.0 ± 1.4
Age, range	80–89	80–89	80–89	90–99	90–98	90–99	100–107	100–103	100–107
Living arrangements, *n* (missing)	56	28	28	46 (2)	12	34 (2)	56	10	46
Alone (%)	7 (12.5)	2 (7.1)	5 (17.9)	3 (6.25)	1 (8.3)	2 (5.6)	1 (1.8)	0 (0.0)	1 (2.1)
With family (%)	46 (82.1)	25 (89.3)	21 (75.0)	32 (66.7)	9 (75.0)	23 (63.9)	41 (73.2)	8 (80.0)	33 (71.7)
With spouse	16	13	3	7	6	1	0	0	0
With biological child	15	9	6	14	2	12	26	6	20
Multigenerational housing 1	14	3	11	9	1	8	9	1	8
Multigenerational housing 2	1	0	1	2	0	2	6	1	5
Institution (%)	3 (5.3)	1 (3.6)	2 (7.1)	13 (27.1)	2 (16.7)	9 (25.0)	14 (25.0)	2 (20.0)	12 (26.1)
Functional ability, *n* (missing)	52 (6)	27 (1)	25 (3)	47 (1)	11 (1)	36	55 (1)	10	45 (1)
Barthel Index, mean ± SD	86.7 ± 27.0[†]	77.1 ± 30.9	88.7 ± 21.2	63.5 ± 31.2[†]	91.8 ± 15.2[‡]	54.9 ± 29.7[‡]	44.2 ± 33.9[†]	48.5 ± 39.4	43.3 ± 33.0
Independent A % (100)	53.8	44.4	64.0	23.4	72.7	8.2	7.3	18.2	4.6
Independent B % (80–99)	15.4	18.5	12.0	12.8	9.1	13.9	16.4	27.3	13.6
Minimal help % (60–79)	15.4	14.8	16.0	27.7	18.2	30.6	18.2	0.0	22.7
Partially dependent % (40–59)	3.9	7.4	0.0	10.6	0.0	13.9	9.1	0.0	11.4
Very dependent % (20–39)	7.7	7.4	8.0	19.1	0.0	25.0	18.2	27.3	15.9
Totally dependent % (<20)	3.9	7.4	0.0	6.4	0.0	8.3	30.9	27.3	31.8
Lawton and Brody IADL, mean ± SD[§]		3.5 ± 1.7	5.8 ± 3.0		4.0 ± 1.2	1.6 ± 1.7		1.3 ± 1.6	1.3 ± 1.9
Smoking status, *n* (missing)[¶**]	52 (4)	28	24 (4)	46 (2)	12	34 (2)	55 (1)	10	45 (1)
Current smoker	7	6	1	1	1	0	0	0	0
Ex-smoker	16	14	2	7	6	1	7	5	2
Never smoker	29	8	21	38	5	33	48	5	43

[†]For total Barthel Index (BI) scores, $P < 0.001$. [‡]For male vs female mean BI scores, $P < 0.0001$. [§]Male and female total instrumental activities of daily living (IADL) scores by age groups, $P < 0.001$. [¶]Gender differences in smoking status by age, $P < 0.001$. **For smoking status by age, $P < 0.0001$. [††]Proportion of females increases by age, $P < 0.0001$. SD, standard deviation.

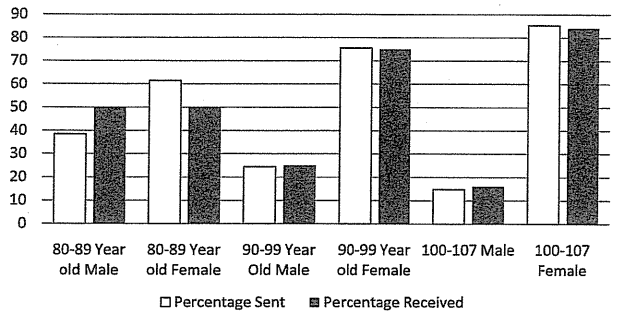

Figure 1 Response rates by age and sex. Open bars denote percentage of questionnaires sent by age and sex groups. A total of 405 questionnaires were sent, 135 to each age group of 80–89, 90–99, and 100–107 year olds. Closed bars denote the percentage of questionnaires received by age and sex groups. A total of 160 questionnaires including 56, 48 and 56 questionnaires by 80–89, 90–99 and 100–107 year olds, respectively, were received.

disorders, osteoporosis, breast cancer and depression at the time of the questionnaire. Other respondents reported past histories of stroke, lung disease, breast cancer and heart attacks. In contrast, a small number of respondents reported continued independence, wellness, and freedom from major illnesses and dementia. Some centenarians reported continuing driving, shopping, sightseeing and attending university classes.

Less than 25% of centenarians in this study reported care beginning before the age of 92 years while 12.1% began receiving care after their 100th birthday (mean age when care began 95.0 ± 5.5 years). Over 75% of centenarians reported receiving care for less than 10 years, the shortest being 11 months and the longest being over 23 years.

Most centenarians (75%) lived in their own private home. Among community-dwelling elderly, 97.6% (41/42) of centenarians lived in family and multigenerational households. The prevalence of third generational families, which include children, grandchildren and great grandchildren, increased with the age of the care respondent. Second generational families, which included children and grandchildren, were more prevalent than third generational families in homes containing a centenarian. One centenarian lived independently and no centenarians had a living spouse. The rates of institutionalization increased with respondent age ($P < 0.001$) though the ratio of institutionalized to community-dwelling centenarians is slightly less than 90–99 year olds.

An application for LTCI had been made by 75% of centenarians (42/56) compared to less than 57% of controls (Fig. 2a). Two of the 42 centenarians who applied for LTCI did not qualify to receive assistance. A total of 16 centenarians (28.6%), 10 whom lived with their biological children, did not have a LTCI support or care needs level.

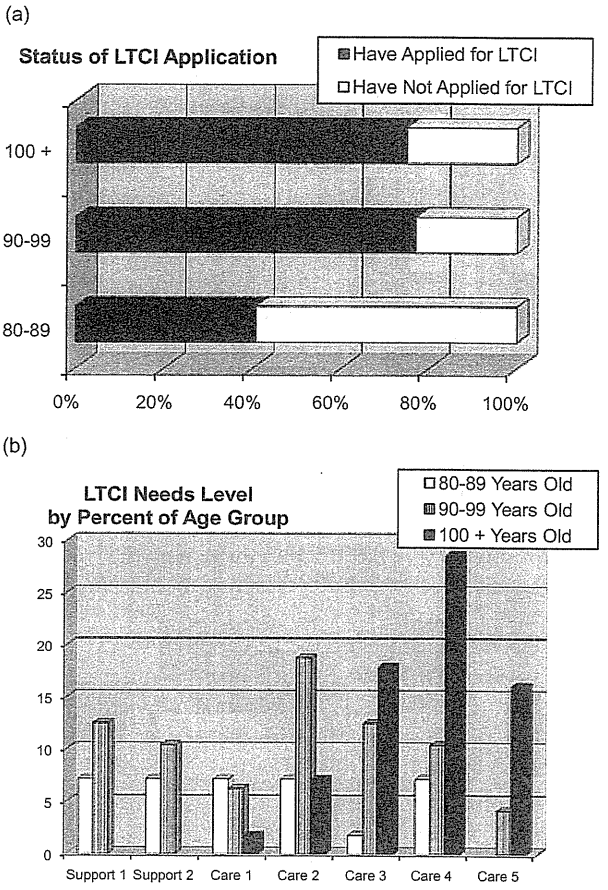

Figure 2 Status of Long-Term Care Insurance (LTCI) by age. (a) Status of applications for LTCI. Open bars show individuals who had not applied for LTCI while closed bars show individuals who had applied for LTCI. Respondents were 80–89 ($n = 54$), 90–99 ($n = 48$) and 100–107 years old ($n = 56$). (b) Percentage of respondents by age group who were eligible for LTCI according to their LTCI care needs level. Open bars represent 80–89-year-old respondents ($n = 13$), closed bars represent 90–99-year-old respondents ($n = 25$), and striped bars represent 100–107-year-old respondents ($n = 40$). Care needs levels range from Support 1, those who are eligible to receive the least amount of services, to Care 5, those who are eligible to receive the maximum amount of services.

The number of respondents who qualified to receive a LTCI support or care needs level increased with age among control recipients ($P < 0.005$) (Fig. 2b). More than 71% of centenarians qualified for LTCI compared to less than 38% of 80–89 year olds who received a support or care needs level and were eligible to utilize LTCI assistance ($P < 0.001$). Centenarians were five times more likely to receive higher care level numbers than 80–89-year-old recipients and three times more likely than 90–99-year-old recipients.

Centenarians were more likely to receive care regularly and to receive LTCI services ($P < 0.001$). Over 73% of centenarians received care regularly. Of the 70% of centenarians (39/56) who reported receiving insurance services, 20.5% (8/39) also received private services. Forty percent more centenarians used LTCI services than 80–89 year olds.

Care needs level beneficiaries receiving care regularly significantly correlated with an increase in recipient age from 52% of 80–89 year olds to over 90% of centenarians ($P < 0.001$). More than 87% of centenarians with LTCI care needs levels receive LTCI services compared to 71.4% of 80–89 and 66.6% of 90–99-year-old controls ($P < 0.004$).

Over 58% of centenarians reported receiving informal care compared to 35.6% of controls ($P < 0.001$). Those receiving informal care were more likely to also receive LTCI services ($P < 0.001$), private services ($P < 0.01$) and care regularly ($P < 0.001$) than those who did not receive informal care. Fewer Independent centenarians (30.7%) reported receiving informal care compared to over 74% of Dependent centenarians ($P < 0.001$).

Centenarians reported receiving 15 different formal services (Fig. 3a) and 17 informal services (Fig. 3b). LTCI services were primarily focused on ADL (41%) followed by medical (37%) and IADL (22%). Informal services focused mainly on IADL (57%) followed by ADL (39%) and medical (4%).

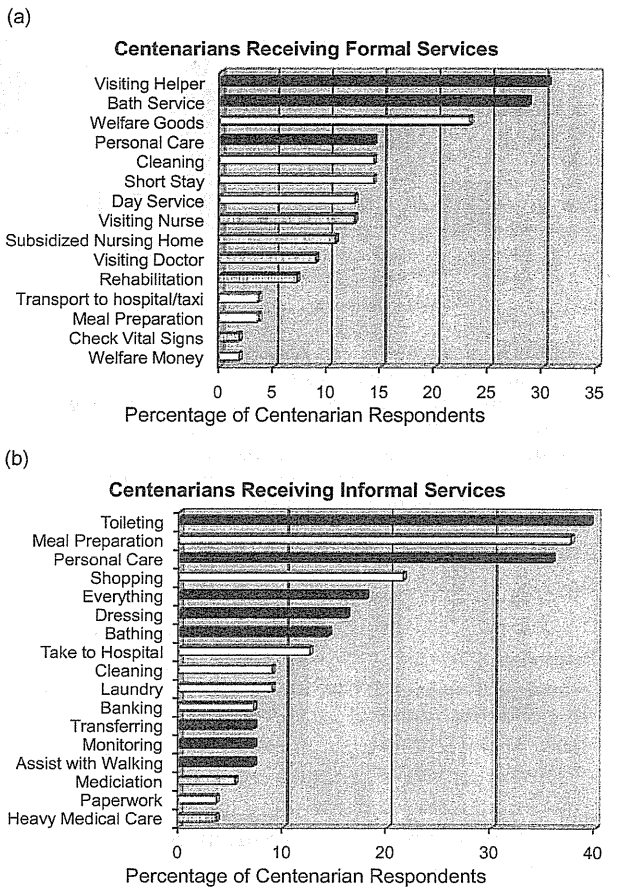

Figure 3 Percentage of centenarians who utilize various formal and informal services. (a) Percentage of indicated formal services including services subsidized by LTCI and privately paid services. (b) Percentage of centenarians receiving the indicated informal services. For both (a) and (b), categories of activities of daily living (ADL) services are denoted by closed bars, categories of instrumental activities of daily living (IADL) services denoted by open bars include day service (senior day care centers which provide various activities ranging from recreation and social activities for individuals with high ADL functioning to rehabilitation and bathing for individuals with lower ADL functioning), receive welfare goods (which include provision of subsidized care equipment such as automatic beds, raised toilet seats, wheelchairs, walkers and hand rails), short stay (which are limited duration programs which include overnight accommodation at a facility, primarily designed for caregiver relief, where the individual returns to their private home after a short period) and paperwork (paperwork related to coordination and payment of care services), and medically oriented services shown in vertically striped bars include subsidized nursing home (LTCI provides some money for institutional fees) and heavy medical care (tube drainage and tube feeding). Percentages of centenarian users are shown.

Discussion

Centenarians in the current study represent a diverse group of individuals ranging from functionally independent to completely dependent and comatose supporting previous research by Evert *et al.*[8] who categorized centenarians into three groups: delayers, escapers and survivors. Some centenarians in this study reported continuing to function autonomously suggesting possible escape from age-associated illnesses which would have limited their ability to continue IADL and supporting previous findings that dementia in centenarians is not inevitable.[9] Individuals who began receiving care after 92 years may have delayed the onset of age-associated illnesses supporting the compression of morbidity hypothesis[10] while others who live with various diseases or disorders may be survivors. Three centenarians reported receiving care for over 20 years, further suggesting the existence of centenarians who survive to advanced age while suffering from disease.

Male 90–99 year olds exhibited higher functional abilities than 80–89 year old and centenarian respondents suggesting that males who live longer are physically healthier than their female counterparts. This supports the gender cross-over phenomenon described by Ohrui *et al.*[11] suggesting that physically weaker males died at younger ages and only the physically strongest males are able to survive to advanced old age while females continue to survive with more physical impairments. The gender cross-over effect in this study peaks in 90–99 year olds and is greatly reduced among centenarians. Although centenarian males comprise the

minority of centenarians, they continue to have higher BI and IADL scores than females. Interpretations of gender cross-over are limited, however, due to the small sample size of males aged 90–99 years old.

This study suggests, but due to the limited size of 90–99 year old males is unable to confirm, previous findings by Perls[12] that male centenarians tend to be better off than female centenarians in terms of physical functioning and that females seem to be physiologically stronger in old age and more likely than males to be able to live with chronic illnesses and disabilities.

While other studies have focused upon centenarians gathered on a certain date,[13] this was impossible in the present study due to the subject demographic collection methods in Japan. The principal investigator S. F. obtained centenarian and control subject data by manually searching over 1 million names printed in city registrar books stored at seven local city offices. This process took 3 months during which the registrar books were not updated.

In this study, two centenarians failed to qualify for LTCI services. By denying LTCI certification it is implied that the individual has high physical and mental abilities. However, the BI level of one of the centenarians denied certification is partially dependent and may suggest misevaluation. It is vital that measurement tools for LTCI eligibility be adjusted to effectively evaluate the centenarian population.

Multigenerational households are more prominent in Japan than other industrialized countries. In Japan, 8.5% of households are multigenerational[14] in contrast to 3% in Great Britain.[15] Multigenerational households may affect the lower levels of institutionalization found in this study as nearly 10% of centenarians in this study live in multigenerational housing. The New England Study found 27% of centenarians lived with family[16] compared to over 71% in this study. Sendai City reports a high proportion of family and multigenerational housing suggesting continuation of traditional cultural practices of aging parents living with their children. Although the rate of institutionalized Japanese centenarians in this study is much less than the 61% found in the New England study, only one centenarian reported living alone compared to 12% in the USA.[16] Low levels of institutionalization reported in this survey may also be affected by the inability of institutionalized care recipients to provide informed consent or refusal by families to report the institutionalization of a family member. In Japan, when a family member enters an institution it is common to keep the registered address as a private residential address and not to change it to an institutional address to avoid social stigmas and therefore it is possible that some of the questionnaires did not reach the elderly person due to incorrect addresses.

The recruitment of centenarians can be extremely difficult. In a study by Hirose *et al.*, of the approximately 1800 centenarians available for study, only 273 agreed to participate, representing a sample size of 15.2%.[17] Moreover, in a study by Shimizu *et al.*, only 22% of the total centenarians in Tokyo were included for study.[18] In contrast, this study reports a centenarian participation rate in Sendai City of 41.5%, double that of Shimizu *et al.*, and more than three times that of Hirose *et al.*[17,18]

The overall participation rate was expected due to multiple unavoidable factors including; high centenarian mortality rate, cognitively impaired individuals inability to provide informed consent, questionnaire length and the slow updating of city registrars.

Although every effort was made to minimize selection bias, it may be unavoidable due to methodological limitations of the questionnaire study protocol. Permission for this study from the Japanese Ministry of Justice and from Sendai City Office permitted only a one-time questionnaire and introduction letter to be sent to selected participants. The researchers were prohibited from contacting respondents by phone, in person visit or follow-up correspondence due to restrictions under Japanese law.

Data gathered may be limited in size and by response rate, however, these are an invaluable resource as this is the first study to provide insight into the situation of centenarians in northern Japan and is an excellent opportunity to increase understanding of how the oldest old utilize the new LTCI program.

In conclusion, centenarians represent a diverse group of individuals with distinctive needs. Centenarians can be classified into various groups suggesting numerous paths to attaining longevity. Gender cross-over, most prevalent among 90–99 year olds, decreased among centenarians. It is possible individuals have been misevaluated under the LTCI program and investigation is needed to determine if the LTCI system effectively assesses centenarians. This is the first in-depth look into the actual situation of community-dwelling oldest old in northern Japan examining functional ability and care service utilization.

By increasing understanding of the health needs of centenarians, government officials can target future health-care services to prepare for the increasing demands from this growing population. Future investigation of centenarians should focus upon the reasons for applying or not applying to LTCI, medical history, family and genetic profiles, and satisfaction with the health-care system.

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Green tea consumption is associated with depressive symptoms in the elderly[1–3]

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ABSTRACT

Background: Green tea is reported to have various beneficial effects (eg, anti–stress response and antiinflammatory effects) on human health. Although these functions might be associated with the development and progression of depressive symptoms, no studies have investigated the relation between green tea consumption and depressive symptoms in a community-dwelling population.

Objective: The aim of this study was to investigate the relations between green tea consumption and depressive symptoms in elderly Japanese subjects who widely consumed green tea.

Design: We conducted a cross-sectional study in 1058 community-dwelling elderly Japanese individuals aged ≥70 y. Green tea consumption was assessed by using a self-administered questionnaire, and depressive symptoms were evaluated by using the 30-item Geriatric Depression Scale with 2 cutoffs: 11 (mild and severe depressive symptoms) and 14 (severe depressive symptoms). If a participant was consuming antidepressants, he or she was considered to have depressive symptoms.

Results: The prevalence of mild and severe and severe depressive symptoms was 34.1% and 20.2%, respectively. After adjustment for confounding factors, the odds ratios (95% CI) for mild and severe depressive symptoms when higher green tea consumption was compared with green tea consumption of ≤1 cup/d were as follows: 2–3 cups green tea/d (0.96; 95% CI: 0.66, 1.42) and ≥4 cups green tea/d (0.56; 95% CI: 0.39, 0.81) (*P* for trend: 0.001). Similar relations were also observed in the case of severe depressive symptoms.

Conclusion: A more frequent consumption of green tea was associated with a lower prevalence of depressive symptoms in the community-dwelling older population. *Am J Clin Nutr* 2009; 90:1615–22.

INTRODUCTION

Depression in late life is a recognized public health problem. Depression can increase the risk of medical illnesses, worsen the outcome of other medical illnesses, and even increase mortality (1, 2).

Many risk factors are recognized as contributors to the occurrence of depressive symptoms. Stress is particularly well established as a factor that can cause depressive symptoms or contribute to the severity of depression (3). Inflammation also is of key importance for central and peripheral hormonal secretion; it also interacts with neurotransmitters and is related to pathophysiologic processes such as neurodegeneration (4). Epidemiologic studies of patients and community dwellers have shown that inflammatory proteins are associated with depressive symptoms (5).

In Asia, green tea, a widely consumed beverage, has been regarded for centuries to possess significant health-promoting effects (6). Many animal studies have suggested that theanine, one of the major amino acids contained in green tea, has a tranquilizing effect on the brain (7). A laboratory study on acute stress showed that the oral intake of theanine lowered the stress response in human participants (8). Several experimental and animal studies have also shown that green tea is an antiinflammatory agent and that it ameliorates the overproduction of proinflammatory cytokines and mediators (9–11). These effects have been attributed largely to the most prevalent polyphenol contained in green tea, catechin, or flavanol (−) epigallocatechin-3-gallate (12).

Thus, we hypothesized that green tea might have a beneficial effect in the primary and secondary prevention of depressive symptoms or psychological distress due to its antagonistic effects on the stress response and inflammation. However, to the best of our knowledge, only a few studies have reported relations between green tea consumption and mental health (13, 14), and a relation concerning depressive symptoms does not appear to have been investigated. Thus, the relation between green tea

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consumption and depressive symptoms in community-dwelling elderly adults, in whom this condition is highly prevalent, remains unclear. In the present study, we investigated the relation between green tea consumption and depressive symptoms in elderly Japanese subjects who consume green tea.

SUBJECTS AND METHODS

Study participants

Our study population comprised subjects aged ≥70 y who resided in the Tsurugaya area of Sendai city, one of the major cities in the Tohoku area of Japan (15, 16). At the time of the study in 2002, there were 2730 individuals aged ≥70 y living in Tsurugaya. All of them were invited to participate in a comprehensive geriatric assessment, which included physical function, cognitive function, and dental status. Of those invited, 1198 participated in the survey and 1178 provided their informed consent for data analysis. The protocol of this study was approved by the Institutional Review Board of the Tohoku University Graduate School of Medicine.

In this study, the depressive symptoms were assessed by using the Geriatric Depression Scale (GDS). Of the 1178 subjects, 1169 completed the GDS (**Figure 1**). Those who did not have any information on diet were excluded (n = 94). Furthermore, subjects who reported cognitive dysfunction (Mini-Mental State Examination score: <18; n = 17) (17) were also excluded. As a result of these exclusions, the final study population comprised 1058 subjects (mean ± SD age: 75.9 ± 4.7 y; men: 42.6%).

Assessment of depressive symptoms

Depressive symptoms were assessed according to the Japanese version (18) of the 30-item GDS. The score ranged from 0 to 30, with greater values indicating increased severity. In this study, 2 cutoffs were used to define different levels of depressive symptoms. The first cutoff was a GDS score ≥11 and/or the use of antidepressants, which indicated relatively mild and severe depressive symptoms. The second cutoff was a GDS score ≥14 and/or the use of antidepressants, indicating relatively severe depressive symptoms.

Assessment of dietary intake

The participants were instructed to fill out a brief self-administered diet-history questionnaire that included 75 food items with specified serving sizes described by natural portions or standard weight and volume measures of the servings commonly

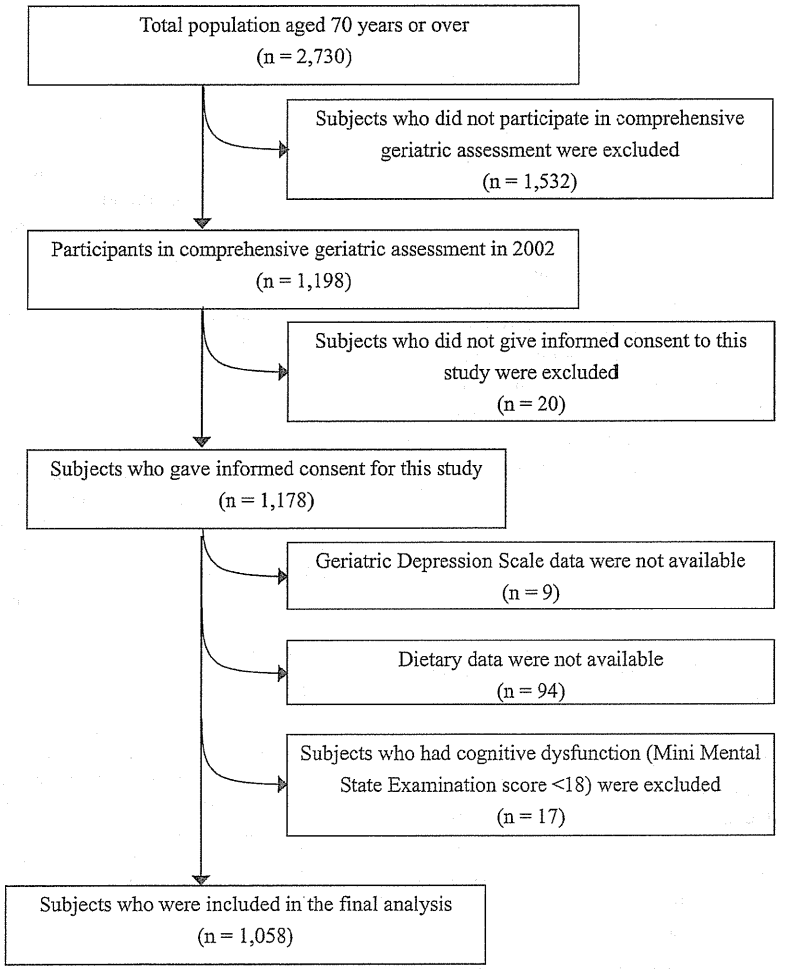

FIGURE 1. Flow chart of the sample selection.

consumed in the study population. The mean daily intake of nutrients was calculated by using an ad hoc computer program developed to analyze the questionnaire. The Japanese food composition tables (19) and others (20) were used as the nutrient database. The reproducibility and validity of the brief self-administered diet-history questionnaire have already been described in detail elsewhere (21).

Participants indicated the mean frequency of consumption of green tea, black or oolong tea, and coffee over the previous 1 mo in terms of the specified serving size by selecting 1 of the 8 frequency categories: almost never, <1 cup/wk, 1 cup/wk, 2–3 cups/wk, 4–6 cups/wk, 1 cup/d, 2–3 cups/d, and ≥4 cups/d. In the study region, the volume of a typical cup of green tea is 100 mL. We summarized these categories in tertile in the following way: green tea (≤1 cup/d, 2–3 cups/d, and ≥4 cups/d), black or oolong tea (almost never, <1 cup/d, and ≥1 cups/d), and coffee (almost never, <1 cup/d, and ≥1 cups/d).

Assessment of other variables

Blood pressure (BP) was measured at home with an HEM747IC device (Omron Life Science Co Ltd, Tokyo, Japan), which uses the cuff oscillometric method to generate a digital display of systolic and diastolic BPs. The mean (±SD) of 15.6 ± 10.4 BP measurements was used as the BP value. Participants who did not measure BP at home on ≥3 d were treated as having missing information on hypertension. Hypertension was defined as a home systolic BP ≥135 mm Hg or a home diastolic BP ≥85 mm Hg or the use of antihypertensive agents (22).

Blood samples were drawn from the antecubital vein, with minimal tourniquet use, while subjects were seated. Specimens were collected in siliconized vacuum glass tubes containing sodium fluoride for blood glucose and no additives for C-reactive protein (CRP) analyses. Blood glucose concentration was measured by using enzymatic methods (Shino-Test, Tokyo, Japan). Diabetes was defined as a casual blood glucose concentration of ≥200 mg/dL or the current use of antidiabetic medication. Highly sensitive CRP concentrations were determined by an immunotechnique that uses a Behring BN II analyzer (Dade Behring, Tokyo, Japan). The BN II assay utilizes a monoclonal antibody coated on polystyrene particles and fixed-time kinetic nephelometric measurements. The detection limit of this assay is 0.02 mg/L. We categorized the study participants on the basis of proposed cutoffs for CRP as low (<1.0 mg/L) or high (at least 1.0 mg/L) (23). The drug information was confirmed by a well-trained pharmacist.

The anthropometric variables (height and body weight) were recorded by using a standard protocol. Body mass index was calculated as weight in kilograms divided by height in meters squared. The sociodemographic variables, which include sex, age, educational level, marital status, cohabitants, perceived social support, and visiting friends, were also assessed. The educational level was assessed by determining the age at completion of schooling and was divided into 2 categories: ≤12 or >12 y (24). Marital status was categorized as follows: married, divorced or widowed, or single. The subjects were also classified as living alone or living with others. Perceived social support (PSS) was evaluated on the basis of the responses (yes or no) to the following 5 questions: "Do you have someone to talk to when you are in trouble?" (PSS1); "Do you have someone to talk to when your physical condition is not good?" (PSS2); "Do you have someone to help you with daily housework?" (PSS3); "Do you have someone to take you to the hospital when you are not feeling well?" (PSS4); and "Do you have someone to take care of you when you are ill and in bed?" (PSS5). These questions were extracted from a previous study on social support and depression among elderly individuals in a rural community (25). A single score was calculated by adding the scores of PSS1–5. The lack of PSS was defined as a PSS score of 0. "Visiting friends" was evaluated on the basis of the responses (yes or no) to the following question: "Do you visit your friends?"

The health-related variables included history of physical illness, pain, cognitive function, instrumental activities of daily living (IADLs), and current medication use. History of physical illness was evaluated on the basis of the responses (yes or no) to questions concerning the history of stroke, ischemic heart disease, cancer, and arthritis. Pain within the previous 4 wk was assessed on the basis of the question, "Have you had any pain recently? If so, how intense was it?" The possible answers were "no pain," "very mild pain," "mild pain," "moderate pain," and "severe pain." Subjects who reported "mild" to "severe" pain were considered to have pain. Cognitive function was assessed with the Mini-Mental State Examination, and scores were classified as belonging to 1 of 3 categories: 18–23, 24–27, and ≥28. The IADL scores were assessed by using the Rouken-Shiki scale (26), and a cutoff of 10/11 was used to determine impairment in IADLs (27).

Information on the smoking ("never," "former," and "current smoking") and drinking ("never," "former," and "current drinking") status of the participants was obtained from a questionnaire survey. Physical activity (PA) was first assessed by a self-reported single question on whether the participant had any PA in the past year. If "yes," further questions were asked about the frequency and duration of walking, brisk walking, and sports. PA was then classified into 3 categories on the basis of the frequency and duration of participation: *1*) "high" (PA ≥3–4 times/wk for ≥30 min each time), *2*) "low" (reporting some PA in the past year, but not enough), and *3*) "none" (no PA). Furthermore, PA was classified into 6 levels on the basis of the above 3 categories and the nature of the physical activity, such as walking, brisk walking, and sports: *1*) level 1 (no walking, brisk walking, or sports), *2*) level 2 (low walking, no brisk walking, no sports), *3*) level 3 (high walking, no brisk walking, no sports), *4*) level 4 (any walking, low brisk walking, no sports), *5*) level 5 (any walking, high brisk walking, no sports), and *6*) level 6 (any walking, any brisk walking, low or high sports). Detailed information has been provided in previous reports (28).

Statistical analysis

The descriptive data have been presented as the mean (with 95% CIs) or as percentages. Depressive symptoms were used as dependent variables, and green tea consumption categories in tertile were used as independent variables. The differences of variables among the green tea consumption categories were examined by analysis of variance for continuous variables or by logistic regression analysis for variables of proportion. For model 1, multiple logistic regression analysis was used to examine relations between green tea consumption and depressive symptoms with adjustment for age; sex; body mass index;

hypertension; diabetes; history of cardiovascular diseases, cancer, or arthritis; high C-reactive protein (≥1.0 mg/L); history of smoking and drinking habits; physical activity (all 6 levels as a categorical variable); cognitive status; impaired IADLs; self-reported body pain; educational level; living alone; and marital status (model 1). For model 2, all of the above variables were used, in addition to serum albumin concentration, total energy intake, intakes per 2000 kcal of energy intake as protein and folate, and consumption frequencies of black or oolong tea (almost never, <1 cup/d, and ≥1 cups/d) and coffee (almost never, <1 cup/d, and ≥1 cups/d). For model 3, all variables in models 1 and 2 in addition to lack of PSS and visiting friends were included. The final multivariate logistic analysis was performed with the forced entry of all factors considered to be potential covariates. Bonferroni-corrected *P* values were used for comparisons between groups differing in green tea consumption. All *P* values for linear trends were calculated by using the categories of green tea consumption (≤1 cup/d: 1; 2–3 cups/d: 2; ≥4 cups/d: 3). The interactions between green tea consumption and all confounders for having depressive symptoms were tested through the addition of the cross-product terms to the regression model. A difference was defined to be significant when $P < 0.05$. All statistical analyses were performed by using the Statistical Analysis System 9.1 edition for Windows (SAS Institute Inc, Cary, NC).

RESULTS

On the basis of the data obtained from 1058 subjects, 34.1% (361/1058) [27.3% (123/451) of men and 39.2% (238/607) of women] were classified as having mild and severe depressive symptoms and 20.2% (214/1058) [14.9% (67/451) of men and 24.2% (147/607) of women] were classified as having severe depressive symptoms.

The participant characteristics according to their green tea consumption status are presented in **Table 1**. The proportion of women, those with a history of cancer, nonsmokers, visiting friends, and widowed (or divorced) status were significantly higher across the green tea consumption tertiles (*P* for trend: <0.0001, 0.04, <0.0001, 0.0001, and 0.02, respectively). The proportion of subjects with a history of cardiovascular disease, who were current smokers or ex-smokers, who were married, and who had impaired IADLs, self-reported body pain, and lack of perceived social support was significantly lower across the categories of green tea consumption (*P* for trend: <0.01, 0.02, <0.0001, <0.01, 0.01, 0.03, and 0.04, respectively). Although the difference was not statistically significant, the proportion of nondrinkers was highest in categories with the lowest green tea consumption. The mean folate consumption ($\mu g \cdot d^{-1} \cdot 2000$ kcal) was significantly higher across categories of green tea consumption (*P* for trend < 0.0001). The mean GDS score was significantly lower across the categories of green tea consumption (*P* for trend < 0.0001). There were no apparent associations between high CRP and green tea consumption. Otherwise, no significant difference was observed between categories of green tea consumption.

The adjusted association between categories of green tea consumption and mild and severe or severe depressive symptoms is shown in **Table 2**. The ORs of the depressive symptoms decreased across categories of green tea consumption. In the final multivariate logistic models, the adjusted ORs for mild and severe depressive symptoms across categories of green tea consumption were 1.00 (reference) for ≤1 cup/d, 0.96 (95% CI: 0.66, 1.42) for 2–3 cups/d, and 0.56 (95% CI: 0.39, 0.81) for ≥4 cups/d (*P* for trend < 0.001). The prevalence of depressive symptoms was 44% lower for participants who consumed ≥4 cups green tea/d tea than for those who consumed ≤1 cup/d (Bonferroni-corrected *P* value <0.01). The ORs of mild and severe depressive symptoms for CRP were 1.00 (reference) for low CRP (<1 mg/L) and 1.08 (95% CI: 0.79, 1.48) for high CRP (≥1.0 mg/L). Similar relations were observed even when we used GDS ≥14 and the use of antidepressants as a definition of depressive symptoms. When we analyzed the relation between the consumption of other beverages and depressive symptoms, a weak or null relation was observed between the consumption of black or oolong tea or coffee and prevalence of depressive symptoms. The multivariate ORs for mild and severe depressive symptoms according to the frequencies of black or oolong tea consumption were 1.00 (reference) for almost never, 0.82 (95% CI: 0.56, 1.20) for <1 cup/d, and 0.71 (95% CI: 0.49, 1.02) for ≥1 cups/d (*P* for trend: 0.06), whereas those for coffee were 1.00 (reference) for almost never, 1.01 (95% CI: 0.73, 1.39) for <1 cup/d, and 0.82 (95% CI: 0.53, 1.27) for ≥1 cups/d (*P* for trend: 0.49). Similar results were also observed when the cutoff ≥14 or the use of antidepressants was used to indicate severe depressive symptoms. Eighteen participants consumed antidepressants in this study. Because individuals who were taking monoamine oxidase inhibitors may have been instructed to avoid the intake of green tea, our findings may have been affected. Therefore, we also analyzed the relations between green tea consumption and depressive symptoms in participants not consuming antidepressants. However, this exclusion did not alter our findings. ORs (95% CI) for mild and severe and for severe depressive symptoms across the green tea consumption tertiles were 1.00, 0.96 (95% CI: 0.67, 1.45), and 0.59 (95% CI: 0.40, 0.87) (*P* for trend < 0.01) and 1.00, 0.97 (95% CI: 0.61, 1.54), and 0.51 (95% CI: 0.32, 0.81) (*P* for trend < 0.01), respectively. We observed a similar relation between green tea consumption and depressive symptoms when men and women were separately analyzed. In model 3, the adjusted ORs (95% CI) for mild and severe and for severe depressive symptoms across the categories of green tea consumption were as follows: for men, the values were 1.00, 0.78 (95% CI: 0.41, 1.48), and 0.45 (95% CI: 0.22, 0.91) (*P* for trend: 0.03) and 1.00, 0.96 (95% CI: 0.44, 2.12), and 0.35 (95% CI: 0.14, 0.87) (*P* for trend: 0.02), respectively; for women, the values were 1.00, 1.09 (95% CI: 0.64, 1.86), and 0.65 (95% CI: 0.40, 1.05) (*P* for trend: 0.04) and 1.00, 0.83 (95% CI: 0.46, 1.49), and 0.50 (95% CI: 0.29, 0.87) (*P* for trend: <0.01), respectively. We did not observe significant interaction between green tea consumption and sex either for mild and severe or for severe depressive symptoms (*P* for interaction: 0.29 for mild and severe and 0.80 for severe). The tests for interaction between the consumption of green tea and other confounders in the final models were also not statistically significant.

DISCUSSION

The present study examined the relation between green tea consumption and depressive symptoms among a community-

TABLE 1
Subject characteristics according to categories of green tea intake[1]

	Categories of green tea intake			
	≤1 cup/d	2–3 cups/d	≥4 cups/d	*P* for trend[2]
n	286	284	488	
Age (y)	75.5 (75.0, 76.1)[3]	76.4 (75.8, 76.9)	75.9 (75.5, 76.3)	0.10
Female sex (%)	48.3	52.8	65.4	<0.0001
BMI (kg/m^2)	23.8 (23.4, 24.2)	23.8 (23.4, 24.2)	24 (23.7, 24.3)	0.80
Serum albumin (g/dL)	4.33 (4.29, 4.36)	4.33 (4.30, 4.36)	4.34 (4.31, 4.36)	0.82
Hypertension (%)	69.6	64.4	70.5	0.61
Diabetes (%)	9.4	8.8	8.8	0.78
History of CVD (%)	19.9	15.9	12.9	<0.01
History of cancer (%)	5.2	4.9	8.8	0.04
History of arthritis (%)	18.5	18.3	17.8	0.80
High CRP (%)[4]	33.9	32.4	31.4	0.46
Smoking status (%)				
Current smoker	16.4	12.7	10.7	0.02
Ex-smoker	39.2	31.0	23.6	<0.0001
Nonsmoker	42.7	55.3	62.9	<0.0001
Drinking status (%)				
Current drinker	41.6	41.2	38.7	0.40
Ex-drinker	14.7	12.0	10.0	0.055
Nondrinker	39.2	44.0	46.3	0.057
PA > level 3 (%)	37.4	41.9	35.3	0.40
Impaired cognitive function (%)				
18 ≤ MMSE < 24	8.4	6.7	7.2	0.58
24 ≤ MMSE < 28	38.5	34.5	34.4	0.29
Impaired IADLs (%)	14.0	15.1	8.4	<0.01
Visiting friends: "yes" (%)	69.6	72.9	81.5	0.0001
Body pain: "yes" (%)	28.0	21.8	20.1	0.01
Lack of perceived social support: total score = 0 (%)	15.7	16.6	10.7	0.03
Educational level ≤12 y (%)	68.2	68.0	71.7	0.26
Living alone: "yes" (%)	22.7	23.9	25.4	0.39
Marital status (%)				
Married	67.1	60.2	59.4	0.04
Widowed or divorced	29.4	34.2	37.5	0.02
Single	3.5	5.6	3.1	0.59
Nutrient intake				
Total energy intake (kcal/d)	1959.9 (1901.3, 2018.5)	2023.9 (1965.2, 2082.7)	1959.6 (1914.8, 2004.4)	0.19
Total protein (g · d^{-1} · 2000 kcal)	82.8 (81.2, 81.2)	81.7 (80.1, 80.1)	83.2 (81.9, 81.9)	0.34
Folate (μg · d^{-1} · 2000 kcal)	336.2 (324.6, 347.8)	372.4 (360.7, 384.1)	404.0 (395.1, 412.9)	<0.0001
GDS scores	9.9 (9.3, 10.5)	9.8 (9.1, 10.4)	8.3 (7.8, 8.8)	<0.0001

[1] CVD, cardiovascular disease; CRP, C-reactive protein; PA, physical activity; MMSE, Mini-Mental State Examination score; IADLs, instrumental activities of daily living; GDS, Geriatric Depression Scale.
[2] Obtained by using ANOVA for continuous variables and logistic regression analysis for variables of proportion.
[3] Mean; 95% CI in parentheses (all such values).
[4] Serum CRP concentrations ≥1.0 mg/L.

dwelling elderly population aged ≥70 y. Our results suggested that high consumption of green tea was significantly related to a lower prevalence of depressive symptoms.

In this large community-based population study, we adjusted for a considerable number of confounding factors. First, we considered that older age, chronic disease, inflammatory status, body mass index, cognitive impairment, disability, lifestyle factors, and psychological problems were potential confounders. However, adjustments for these confounding factors did not change the significant inverse relation between green tea consumption and depressive symptoms. That is, the inverse relation between the frequency of green tea consumption and depressive symptoms was independent of these factors. Second, the effect of the consumption of folate (29) and other beverages such as black or oolong tea or coffee on depressive symptoms was adjusted. Moreover, depressive symptoms can affect hunger and thirst and thus affect nutritional intake (30, 31). Accordingly, we made adjustments for total energy intake, protein consumption, and serum albumin concentration. However, the adjustment for the consumption of these factors also did not change the significant inverse relation between green tea consumption and depressive symptoms. Third, green tea consumption is a unique form of social activity among the Japanese and this, in itself, may influence the depression status. However, the adjustment for perceived social support and visiting friends did not change the significant inverse relation between green tea consumption and depressive symptoms. The association between green tea consumption and the 2 grades (mild and severe and severe) of

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TABLE 2
Adjusted relations between consumption of green tea and mild and severe or severe depressive symptoms[1]

	Categories of green tea consumption			
	≤1 cup/d	2–3 cups/d	≥4 cups/d	*P* for trend[2]
n	286	284	488	
No. of mild and severe depressive symptoms, defined as GDS ≥11 or use of antidepressants	114	111	136	—
Model 1[3]	1.00	0.95 (0.66, 1.36)[4]	0.56 (0.40, 0.78)[5]	<0.001
Model 2[6]	1.00	0.96 (0.66, 1.40)	0.54 (0.37, 0.78)[5]	<0.001
Model 3[7]	1.00	0.96 (0.66, 1.42)	0.56 (0.39, 0.81)[5]	0.001
No. of severe depressive symptoms, defined as GDS ≥14 or use of antidepressants	75	67	72	—
Model 1[3]	1.00	0.91 (0.60, 1.37)	0.48 (0.33, 0.71)[5]	<0.001
Model 2[6]	1.00	0.92 (0.59, 1.42)	0.46 (0.30, 0.72)[5]	<0.001
Model 3[7]	1.00	0.92 (0.59, 1.44)	0.48 (0.31, 0.75)[5]	<0.001

[1] GDS, Geriatric Depression Scale.
[2] Obtained by using multiple logistic regression analysis.
[3] Adjusted for age; sex; BMI; hypertension; diabetes; history of cardiovascular diseases, cancer, or arthritis; high C-reactive protein (≥1.0 mg/L); history of smoking and drinking habits; physical activity (all 6 levels as a categorical variable); cognitive status; impaired instrumental activities of daily living; self-reported body pain; educational level; living alone; and marital status.
[4] Adjusted odds ratio; 95% CI in parentheses (all such values).
[5] Significantly different from green tea consumption of ≤1 cup/d, $P < 0.01$ (Bonferroni-corrected).
[6] Additionally adjusted for serum albumin concentration, total energy intake, intakes per 2000 kcal of energy intake as protein and folate, black or oolong tea consumption, and coffee consumption.
[7] Additionally adjusted for lack of perceived social support and visiting friends.

depressive symptoms was tested in this study. Similar relations were observed consistently in the case of both cutoffs. We also conducted a stratified analysis for sex, and similar relations were also observed when men and women were analyzed separately.

In this study, our primary hypothesis was that green tea may have a potentially beneficial effect on the prevention of depressive symptoms due to its anti–stress response and antiinflammatory effects. However, the antiinflammatory mechanisms were less likely to explain our findings. We did not observe any relations between green tea consumption and CRP. CRP also was not associated with depressive symptoms in this elderly population. Thus, CRP did not explain the inverse relation between green tea consumption and depressive symptoms.

We considered that the other mechanism (ie, the anti–stress response effect) of green tea might explain our findings. Theanine might be a candidate for explaining the observed inverse association between green tea consumption and depressive symptoms. Theanine is one of the major amino acid components in green tea and can pass through the blood-brain barrier (32). Dopamine and serotonin dysfunction is a credible etiological candidate for depressive symptoms (33), and animal neurochemistry studies have suggested that theanine increases the brain serotonin and dopamine concentrations (7). Moreover, theanine is also contained in other kinds of tea, such as black or oolong tea (34). In fact, in the current study, a weak, although not statistically significant, relation was also observed between the consumption of black or oolong tea and the prevalence of depressive symptoms (*P* for trend: 0.06). Thus, these data prove a useful hypothesis that higher consumption of green tea is related to a lower prevalence of depressive symptoms, possibly because it leads to a decrease in the stress response. A further study is required to clarify whether green tea or theanine have a beneficial effect on the prevention and treatment of depressive symptoms.

Our recent findings are also consistent with the present findings. Hozawa et al (13) investigated the relation between the frequency of green tea consumption and psychological distress. The study analyzed 42,093 Japanese individuals aged ≥40 y from the general population residing in the rural area of Japan. The study also showed an inverse relation between the frequency of green tea consumption and psychological distress as assessed by K6 (35). The OR and 95% CI of having psychological distress in subjects who consumed ≥5 cups green tea/d was 0.80 (95% CI: 0.70, 0.91) as compared with the subjects who consumed <1 cup green tea/d after adjustment for the possible confounding factors. The inverse association between green tea consumption and mental ill health was consistently observed whether the population was older (the present study) or middle aged (13), whether urban (the present study) or rural (13), whether being assessed by GDS (the present study) or by K6 (13). We considered that these 2 sets of findings corroborate our conclusion that green tea consumption is associated with mental well-being.

This study has several limitations. First, because the assessments were performed in a public facility, the participants were more active and healthy than those who did not undergo the assessment. Therefore, our results might not represent an elderly general population. Second, the GDS is designed for measuring the intensity of depressive symptoms and not for making a clinical diagnosis of depressive episodes. Therefore, a larger population study that uses a standardized comprehensive structured diagnostic interview should be undertaken to confirm the effect of green tea consumption on depressive symptoms. Third, because this study was a cross-sectional study, we could not conclude whether lower green tea consumption increased the

occurrence of depressive symptoms or whether depressive symptoms lead to a decline in green tea consumption. Therefore, a prospective study or trial should be undertaken to confirm the relation between green tea consumption and depressive symptoms. Fourth, we could not make adjustments for a history of depressive disorders, other psychological variables, and associated medications/supplements because data for these were not obtained. However, because all assessments of this study were carried out in a public facility and participation in the study was voluntary, we considered the prevalence of these factors as likely to have been very low, and therefore we believe that not directly accounting for them in our analyses had little effect on the findings. Moreover, although we adjusted for a considerable number of confounding factors, we cannot exclude the possibility that depressive symptoms are affected by the other dietary habits that correlate with the habitual consumption of green tea. Therefore, an intervention study is necessary for establishing a causal relation between green tea consumption and depressive symptoms.

In the present study, higher green tea consumption (as measured by self-administered questionnaires) was significantly associated with a lower prevalence of depressive symptoms in community-dwelling elderly individuals. This finding suggested that the consumption of green tea may have a potentially beneficial effect on the prevention of depressive symptoms. A prospective study or randomized trials are required to clarify the causality.

The authors' responsibilities were as follows—KN and AH: study concept and design; KN, AH, SK, SE, NN, KO-M, HT, YM, HA, SA, RN, and IT: acquisition of subjects and data; KN, AH, SK, SE, HG, NN, KO-M, HT, YM, MA, SS, HA, SA, and RN: analysis and interpretation of data; KN, AH, HG, and MA: preparation of manuscript; SS, HA, SA, RN, and IT: supervision; and IT: obtaining funding. None of the authors had a conflict of interest.

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