

Fig 3. Survival probability curves for patients with advanced non-small-cell lung cancer treated with nitroglycerin (NTG (+), —) and without nitroglycerin (NTG (-), ---) during chemotherapy. The *P* value was calculated by the log-rank test.

four courses. Additional study is needed to clarify whether there is additional clinical benefit beyond four courses of arm A treatment in patients with NSCLC.

In this study, there were higher rates of adenocarcinoma and of stage IV patients in arm B compared with arm A, although there were no statistically significant differences between the two arms in univariate analysis. Conversely, histological difference and staging of lung cancer were not associated significantly with response to chemotherapy in multivariate analysis with logistic regression analysis. These findings suggest that high rates of adenocarcinoma and stage IV patients in arm B might not contribute to the poorer response

rate for that arm, although the possibility of contribution could not be ruled out.

The effects of NO donors on HIFs and tumor growth without the use of anticancer drugs are controversial.^{17-20,26,27} However, NO-donating drugs such as nitroglycerin might reduce resistance to chemotherapy via improvement of hypoxic conditions,^{10,13,16,21,45-51} reduced HIF-1 stabilization,¹⁷⁻¹⁹ direct effects of NO on cancer cells,^{22-24,52,53} increase in activated p53 protein,^{20,25,54-56} and via an increase in drug delivery in tumor tissue. In this study, plasma levels of VEGF, an HIF-regulated protein,^{38,57} after treatment with nitroglycerin for 3 days were lower than levels before nitroglycerin treatment. These findings suggest that reduced levels of plasma VEGF might be associated with mechanisms regarding an increase in response rate in patients treated with nitroglycerin. However, the number of patients whose plasma VEGF levels were measured was very small (*n* = 6 in each arm), and other HIF-regulated proteins including transforming growth factor alpha and thrombospondin-1⁵⁷ were not examined in this study. Therefore, it is still uncertain what mechanisms contribute to an increase in response rate in patients with NSCLC treated with nitroglycerin. Additional studies are needed to make clear the effects of nitroglycerin.

In summary, this is the first report demonstrating that combinational treatment with nitroglycerin during chemotherapy may enhance the response rate to VC, elongate the TTP, and improve overall survival in patients with advanced stage IIIB/IV NSCLC without major adverse effects in a randomized phase II trial. VC combined with nitroglycerin and VC alone are feasible and have acceptable toxicity profiles. To validate these provocative results, a prospective randomized phase III trial to evaluate nitroglycerin plus VC is underway in patients with stage IIIB/IV NSCLC.

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itation services (home and institutional). Thus, nonmedical reasons largely affected total length of stay, and it is likely that subanalyses would be needed to evaluate the influence of a geriatric intervention. There are increasing data to support combined orthogeriatric care for older people with hip fracture even if not all published reports are consistent,³ although strong evidence derived from large randomized trials is needed in support of this model of care.

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ARTERIAL CARBOXYHEMOGLOBIN CONCENTRATIONS AS A PROGNOSTIC PREDICTOR IN ELDERLY PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG CANCER

To the Editor: Non-small-cell lung cancer (NSCLC) accounts for about 75% of primary lung cancer, which is the leading cause of cancer deaths in industrialized countries. It is desirable to predict a prognosis in elderly patients with NSCLC using a simple and reliable method. Arterial blood carboxyhemoglobin concentration (Hb-CO) is a useful biomarker of disease activity in inflammatory pulmonary diseases and is associated with cancer tissue volume in operable NSCLC.¹⁻⁵ Change in Hb-CO from before chemotherapy to Day 4 of the first cycle of chemotherapy (Δ Hb-CO) in advanced lung cancer was reported to be a good predictor of response to the chemotherapy, with a high sensitivity and a high specificity,⁶ but Δ Hb-CO as a predictor for prognosis in advanced NSCLC has not been reported.

To assess the effects of Δ Hb-CO on survival, 140 patients (mean age \pm standard error 72.4 \pm 0.5; 111 men, 29 women) with advanced NSCLC treated with chemotherapy between October 2000 and April 2003 were studied. No patients in this study were participating in any interventional study. Seventy-three patients had adenocarcinoma (14 patients in Stage IIIB, 59 in Stage IV), 61 had squamous cell carcinoma (22 in Stage IIIB, 39 in Stage IV), and six had large-cell carcinoma (3 in Stage IIIB, 3 in Stage IV). Forty-seven patients were treated with mitomycin 8 mg/m² and cisplatin 80 mg/m² at Day 1 plus vinorelbine 25 mg/m² at Days 1 and 8, 21 patients with docetaxel 60 mg/m² at Day 1 plus gemcitabine 1,100 mg/m² at Days 1 and 8, 45 patients with vinorelbine 25 mg/m² at Days 1 and 8 and cisplatin 80 mg/m² at Day 1, and 27 patients with docetaxel 60 mg/m² at Day 1 plus cisplatin 80 mg/m² at Day 1 every 3 weeks for a maximum of four cycles. A chest computed tomography scan was performed before chemotherapy and after the second and fourth cycles of chemotherapy to estimate the effect of chemotherapy on tumor volume. An independent oncologist evaluated response to chemotherapy according to the criteria of the World Health Organization.⁷ Hb-CO was measured using a spectrophotometer¹⁻⁶ before chemotherapy and at Day 4 of the first cycle of chemotherapy. Current smokers were excluded out by measuring urinary cotinine concentration.¹ The patients were divided into two subgroups: patients with large ($\geq 0.3\%$, Group A) or small ($< 0.3\%$, Group B) Δ Hb-CO relative to an arbitrary cutoff value (0.3%), as described previously.⁶ Survival time was calculated from the date of the start of chemotherapy to the date of death. The Tohoku University ethics committee approved this study, and informed consent was obtained from each subject.

There were no statistically significant differences in baseline characteristics, adverse effects, or treatment delivery between Groups A and B. Δ Hb-CO in Group A was significantly higher than in Group B (0.49 \pm 0.03 vs 0.07 \pm 0.01%, $P < .001$, Student *t* test). The response rate in Group A (95.7%, 44 of 46 patients) was significantly higher than that in Group B (5.3%, 5 of 94) ($P < .001$, chi-square test). The median survival time in Group A was longer than that in Group B (313 vs 242 days). Δ Hb-CO was associated with the prolongation of survival time even after adjustment for age, sex, cancer cell type, cancer staging, and chemotherapy regimen in the Cox regression analysis (hazard ratio = 3.5, 95% confidence interval = 1.8-6.8, $P < .001$). Furthermore, Kaplan-Meier analysis showed that the survival curve of Group A was higher than that of Group B ($P < .001$, log-rank test) (Figure 1).

The close association between large Δ Hb-CO and high response rate to chemotherapy in the present study is consistent with the findings of a previous study.⁶ Carbon monoxide (CO) was reported to inhibit hypoxia-inducible factor-1 (HIF-1) in the hypoxic conditions in solid tumor tissue.⁸ Alternatively, HIF-1 activates the transcription of many genes that code for proteins involved in angiogenesis, cell growth, metastasis, and resistance to chemotherapy.^{9,10} Therefore, the CO molecule of Hb-CO might have beneficial clinical effects on response to chemotherapy. Further study is needed to clarify these mechanisms.

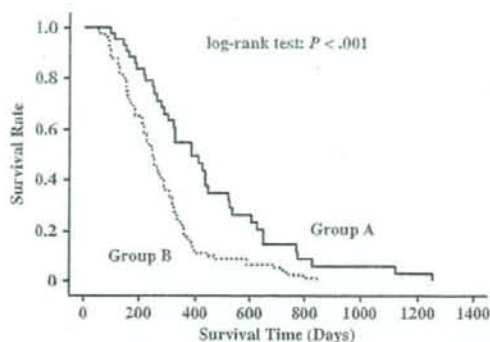


Figure 1. Survival curves in elderly patients with large changes in arterial blood carboxyhemoglobin concentration ($\Delta\text{Hb-CO}$, $\geq 0.3\%$, Group A, solid line) and small $\Delta\text{Hb-CO}$ ($< 0.3\%$, Group B, dotted line) during chemotherapy. *P*-values were calculated using the log-rank test.

In summary, increases in arterial Hb-CO at Day 4 of the first cycle of chemotherapy in elderly patients with advanced NSCLC may be a good prognostic marker.

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CHICKENPOX IN A GERIATRIC PATIENT

To the Editor: In adults, infection from varicella zoster virus (VZV) may present and be accompanied by many complications.^{1,2} We present a case of varicella (chickenpox) infection in an elderly patient with multisystem reactions.

CASE REPORT

An 87-year-old male farmer was admitted in our department complaining of fever (up to 39°C) beginning 3 days before, vertigo, confusional state, and inability to walk. Dementia had been diagnosed 2 years before, and his grandchild had been sick with varicella 10 days earlier. Physical examination was without abnormal findings, except for his mental status. The patient was stuporous, and neurological examination revealed mixed aphasia. Electrocardiogram showed right bundle branch block and sinus rhythm. Cranial computed tomography (CT) scan revealed only leukoencephalopathy and brain atrophy. Thorax x-ray revealed infiltration of the left upper pulmonary lobe, and sputum culture was negative for bacterial infection. Laboratory examination demonstrated mildly elevated the C-reactive protein (3 mg/dL; normal range 0.8-2 mg/dL).

During the second day of hospitalization, and while he was receiving antibiotic therapy for pneumonia, a diminution of the fever and a vesicular rash on the face and upper limbs appearing simultaneously were observed. The next day, the rash had spread to the scalp and whole body (Figure 1A) without return of fever; a Tzanck smear test was performed and found to be positive; immunoglobulin (Ig) M and IgG antibodies for VZV were also found. Antiviral treatment with intravenous acyclovir 10 mg/kg three times a day for 7 days^{3,4} and local treatment with drying anti-

standard treatments.¹⁰ Lately, it has been shown that cyclophosphamide, doxorubicin, vincristine, and prednisone, with the addition of rituximab, is the standard treatment for non-Hodgkin's lymphoma in older people.

In conclusion, despite the perceived barriers to including elderly cancer patients in clinical trials, there are few data to support excluding them. The increasing use of a complete geriatric assessment can lead to a more individualized patient treatment plan. Furthermore, the enormous advances in supportive treatments over recent years enable adverse effects to be minimized. Moreover, the implementation of prospective trials is strongly recommended to assess properly the quality of life of elderly patients undergoing chemotherapy. In this way, it could be possible to counteract an unjustified "ageism": a prejudice that denies opportunities of treatment or even cure for patients that, as far as we know, may have the same chance as younger patients.

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ARTERIAL CARBOXYHEMOGLOBIN CONCENTRATIONS AS A PREDICTOR OF CHEMOSENSITIVITY IN ELDERLY PATIENTS WITH ADVANCED LUNG CANCER

To the Editor: Because the response to anticancer drugs is different in elderly patients with lung cancer, a reliable and simple method¹ to predict the response to chemotherapy is needed. Arterial blood carboxyhemoglobin concentration (Hb-CO) is a useful biomarker of disease activity in inflammatory pulmonary diseases,²⁻⁵ although it has not been reported as a predictor of response to chemotherapy in advanced lung cancer.

One hundred one elderly patients (mean age \pm SE = 70.4 \pm 1.1) with advanced lung cancer treated with chemotherapy were studied. Thirty-five of 101 patients had small-cell lung cancer (SCLC), and 66 had non-small-cell lung cancer (NSCLC). The characteristics of the patients are shown in Table 1. Patients with SCLC were treated with cisplatin 80 mg/m² at Day 1 and etoposide 100 mg/m² at Days 1-3 every 3 weeks for a maximum of four cycles. Patients with NSCLC were treated with mitomycin 8 mg/m² at Day 1, vinorelbine 25 mg/m² at Days 1 and 8, and cisplatin 80 mg/m² at Day 1) or gemcitabine 1,000 mg/m² at Days 1 and 8 and docetaxel 60 mg/m² at Day 1 every 3 weeks for a maximum of four cycles. A chest computed tomography scan was performed before chemotherapy and after the second and fourth cycles of chemotherapy to estimate the effect of chemotherapy on tumor volume. An attending oncologist evaluated response to the chemotherapy according to the criteria of the World Health Organization.⁶ Hb-CO was measured using a spectrophotometer²⁻⁵ before chemotherapy and at Days 4 and 21 of the first cycle of chemotherapy. Current smokers were excluded by measuring urinary cotinine concentrations.^{2,4} The patients were divided into two subgroups: patients with high and low maximum changes in Hb-CO during chemotherapy relative to an arbitrary cutoff value (0.3%) discriminating the responder from the nonresponder in chemotherapy, which was determined using receiver operating characteristic curve analysis with ROCKIT (Windows 95, version 0.9.1 beta, Microsoft, Corp., Redmond, WA). The Tohoku University Ethics Committee approved this study, and informed consent was obtained from each subject.

The response rate was 80% in patients with SCLC and 38% in those with NSCLC. In responder patients with SCLC and NSCLC, Hb-CO increased significantly,

Table 1. Characteristics of Patients with High or Low Carboxyhemoglobin (Hb-CO) Changes

Characteristic	Hb-CO Change					
	Small Cell Lung Cancer			Non-Small Cell Lung Cancer		
	Low (n = 9)	High (n = 26)	P-value	Low (n = 42)	High (n = 24)	P-value
Age, median (range)	71 (61-78)	71 (55-80)	NS	68 (54-84)	70 (55-82)	NS
Male/female, n	9/0	21/5	NS	31/11	19/5	NS
Smoking history, n			NS			NS
Exsmoker	9	24		37	22	
Nonsmoker	0	2		5	2	
Stage, n			NS			<.01
IIIB	2	14		6	13	
IV	7	12		36	11	
Cell type, n			—			NS
Small cell	9	26		—	—	
Squamous cell	—	—		17	9	
Adenocarcinoma	—	—		19	15	
Large cell	—	—		6	0	
Chemotherapy, n			—			<.05
Cisplatin + etoposide	9	26		—	—	
Mitomycin + vinorelbine + cisplatin	—	—		22	20	
Gemcitabine + docetaxel	—	—		20	4	
Hb-CO before chemotherapy, %, mean ± SE	0.99 ± 0.10	0.61 ± 0.03	<.001	0.79 ± 0.03	0.64 ± 0.04	<.01
Maximum change in Hb-CO during chemotherapy, %, mean ± SE	0.08 ± 0.03	0.55 ± 0.04	<.001	0.06 ± 0.01	0.46 ± 0.04	<.001
Tumor shrinkage, cm ³ , mean ± SE	-1.78 ± 2.48	15.23 ± 2.42	<.001	-3.00 ± 1.14	17.16 ± 2.49	<.001
Chemosensitivity			<.001			<.001
Responder	2	26		1	24	
Nonresponder	7	0		41	0	

NS = nonsignificant; SE = standard error.

achieved maximum change at Day 4 of the first cycle of chemotherapy, and then returned to baseline. In contrast, in nonresponder patients with SCLC and NSCLC, Hb-CO did not increase during chemotherapy. Hb-CO before chemotherapy in responders to the chemotherapy was significantly lower than in nonresponders with SCLC ($P < .001$) and NSCLC ($P < .01$) (Student *t* test). Twenty-six of 28 responding patients with SCLC and 24 of 25 responding patients with NSCLC were categorized as patients with high Hb-CO changes. The response rate of patients with high Hb-CO changes was significantly higher than that of patients with low Hb-CO changes, regardless of whether they had SCLC or NSCLC ($P < .001$ for both; chi-square test) (Table 1). Hb-CO correlated significantly with tumor size in patients with SCLC (correlation coefficient (r) = 0.83, $P < .001$) and those with NSCLC ($r = 0.27$, $P < .05$) before chemotherapy. Maximum increases in Hb-CO at Day 4 of the first cycle of chemotherapy were significantly associated with the response to the chemotherapy in patients with SCLC (regression coefficient (RC) = 0.70 (95% confidence interval (CI) = 0.44-0.96, $P < .001$) and those with NSCLC (RC = 1.52, 95% CI = 1.24-1.80, $P < .001$) (multiple regression analysis). For the distinction between nonresponders and responders to chemotherapy, the cutoff value of 0.3% of the maximum increases in the Hb-CO during chemotherapy in patients with SCLC yielded a sensitivity of 95.9% and a specificity of 95.0% and that in

patients with NSCLC yielded a sensitivity of 96.4% and a specificity of 97.0%.

The positive correlation between Hb-CO before chemotherapy and tumor volume in this study is consistent with a previous report.⁷ A hypoxic condition in a solid tumor induces heme oxygenase-1 (HO-1) via an increase in hypoxia-inducible factor-1, which endogenously produces carbon monoxide.^{8,9} Furthermore, resistance to an anti-cancer drug increases with tumor volume, because the increased hypoxia in tumors induces p-glycoprotein related to resistance to anticancer drugs.⁸ Therefore, the increase in Hb-CO before chemotherapy may be associated with low chemosensitivity in lung cancer. A transient increase in Hb-CO during chemotherapy in responders was demonstrated in the present study. The decrease in tumor volume after chemotherapy may be associated with the induction of HO-1 in cancer tissue through generation of reactive oxygen species from apoptotic cancer cells,^{9,10} but the precise mechanism is unknown.

In summary, arterial Hb-CO before chemotherapy in patients with SCLC and increases in arterial Hb-CO at Day 4 of the first cycle of chemotherapy in patients with SCLC and NSCLC may be a predictor of chemosensitivity.

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EVIDENCE-BASED PRESCRIBING OF ANTIRESORPTIVE THERAPY FOR FEMALE NURSING HOME RESIDENTS WITH OSTEOPOROSIS: HOW GOOD IS THE EVIDENCE?

To the Editor: Bone health in nursing home residents and postmenopausal osteoporosis are important.^{1,2} Dr. Jachna et al.³ found that only 20% of nursing facility residents received antiresorptive therapy, which was considered to be underused.³ Two interesting articles among others in the editorial were cited to support the evidence-based prescribing of antiresorptive therapy for nursing home women and therefore to improve the underuse of antiresorptive therapy.⁴ In the first study cited,⁵ 68% of participants were living in continuing-care retirement communities, 12% in retirement communities, 12% in skilled-care nursing homes and residential-care facilities, and 8% in congregate-care facilities. Because the majority of participants were not nursing home residents, the results from this study⁵ might not be applicable to the nursing home setting. Searching PubMed between 1997 and 2005 found no single randomized risedronate trial conducted only in nursing homes. Based on the meta-analysis of the Cochrane Review in the second study cited,⁶ the editorial estimated that taking risedronate for 2 years would prevent 55 vertebral (number needed to treat = 16) and 25 nonvertebral (number needed to treat = 35) fractures,⁴ but the Jadad 5-point scale used for the internal validity of eight randomized risedronate trials of postmenopausal osteoporosis in the non-nursing home setting from the meta-analysis in the second cited study was between 1 of 5 and 5 of 5.⁶ Median Jadad 5-point score was 3 (range 1-5). Using Jadad score to assess the quality of randomized risedronate trials might be unfamiliar to the majority of practicing physicians. Therefore, major items for internal validity of six randomized risedronate trials included in the meta-analysis in the second study cited⁶ (one trial published as an abstract and another in the symposium were excluded) are listed in Table 1. High dropouts could reduce the internal validity of these trials. In addition, most of these trials did not provide methods of randomization and allocation concealment, which is consistent with previous findings.⁷ Poor quality of research has been a major concern.^{7,8} The low quality of trials included in the meta-analyses could lead to significant exaggeration of treatment

Table 1. Selected Internal Validity Indicators of Randomized Risedronate Trials (N = 6)

Indicators	Value
Reporting power calculation, n (%)	3 (50.0)
Described as randomized, n (%)	6 (100.0)
Reporting method of randomization, n (%)	1 (16.7)
Reporting method of allocation concealment, n (%)	1 (16.7)
Described as double blind, n (%)	6 (100.0)
Reporting dropouts, n (%)	6 (100.0)
Dropouts, n, median (range)	280 (15-4,654)
Dropout rate, %, median (range)	37.6 (13.5-49.9)
Jadad score, median (range)*	3 (3-5)

* From the original study.⁶ Jadad score is between 0 and 5.

Attitudes toward disclosing the diagnosis of dementia in Japan

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ABSTRACT

Background: The rapid increase in the elderly population in Japan has triggered a debate on whether or not patients with dementia should be informed of their diagnosis. The purpose of the present study was to investigate the attitudes of people in a large city in Japan toward the disclosure of a diagnosis of dementia.

Methods: In Study 1, 2000 residents aged 40–64 and 5000 residents aged 65 and over were sampled randomly, and a structured questionnaire was sent to them by mail. In Study 2, we administered a structured interview-based questionnaire to 3949 randomly enrolled residents of Nagoya City aged 45 and over whose family member had been certified as needing long-term care.

Results: In Study 1, 79.8% of the younger respondents ($n = 710$) stated that they would prefer the disclosure of a hypothetical diagnosis of dementia, as did 75.5% of the older respondents ($n = 2162$). Furthermore, 85.1% ($n = 749$) of the younger respondents and 82.5% ($n = 2181$) of the older respondents stated that they would prefer that the patient be told his or her hypothetical diagnosis of dementia. In Study 2, in the case of care recipients without dementia, 68.3% ($n = 650$) of their family members preferred disclosure of a hypothetical diagnosis of dementia. Among the families of care recipients who had dementia, 58.4% ($n = 301$) of family members preferred disclosure.

Conclusions: The present survey of caregivers and non-caregivers in an urban city of Japan demonstrated that the desire for disclosure of a diagnosis of dementia is relatively high.

Key words: dementia, diagnosis, long-term care insurance system, adult guardianship

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Introduction

Japan has been experiencing the fastest growth of the elderly population in the world and the percentage of the population aged 65 years old and over finally exceeded 20% in 2006. A mandatory social long-term care insurance system was therefore implemented in Japan in April 2000; all people aged 65 and older are eligible to benefit from institutional and community-based services upon certification of their need for care. In 2003, more than 3.8 million people were certified to receive long-term care insurance benefits in Japan. In parallel with the introduction of long-term care insurance, the adult guardianship law came into effect to shift the system from one of enforcement to one of contract. The law is applied to a person whose mental capacity is impaired due to dementia, mental deficiency or mental illness, and is aimed at securing legal advocacy of his/her own autonomy (Nakatani, 2000).

With the increase in the elderly population, the number of people with dementia is also steadily increasing. Because patients with dementia may be unable to understand the implications of their diagnosis or make decisions on clinical, social or financial issues, their caregivers have a unique role in the process of disclosing the diagnosis of dementia. A growing national concern for older people with dementia, particularly after the introduction of the long-term care insurance system and the increase in the number of people with dementia, has triggered a debate on whether or not patients should be informed of their diagnosis.

The results of previous reports on the opinions of caregivers toward diagnostic disclosure of dementia to the care recipients were largely inconsistent (Bamford *et al.*, 2004). In Japan the results of domestic reports regarding this issue were also in disagreement (Sugiyama *et al.*, 2003; Yamashita *et al.*, 2002). In the present study we surveyed the attitudes of both caregivers and non-caregivers toward the disclosure of a diagnosis of dementia; our subjects were a population sampled in a large city in Japan.

Methods

The study consisted of two protocols, both of which were carried out in Nagoya City, which is located in the central part of Japan. Nagoya City has a population of 2 202 259 (April 2004), of whom 18.0% are 65 years of age or older. This study was developed and organized by Nagoya City and was supported by the Department of Geriatrics of Nagoya University Graduate School of Medicine. Written informed consent was obtained from all participants.

Study 1

Two thousands residents aged 40–64 and 5000 residents aged 65 and over were sampled randomly and a structured questionnaire was sent to them in December 2004. People residing in long-term care facilities and those admitted to hospitals were excluded. The questionnaire asked the participants about their background, their perceptions of dementia, level of anxiety about possible future dementia, awareness of the adult guardianship law and attitude toward the disclosure of a diagnosis of dementia. The care needs of the older participants were also surveyed. In the long-term care insurance system in Japan, all care recipients have their care needs categorized into seven levels [not eligible (independent), need support, and care need levels 1–5] depending on their physical and mental capabilities.

Study 2

We randomly enrolled 3949 residents of Nagoya City aged 45 and over who had been certified as requiring long-term care. Of these participants, 1885 were actively using at least one type of service provided by public long-term care insurance, and 2064 were not currently using any of these services. A structured interview-based questionnaire was administered to the families of the enrolled people by the investigators to evaluate the physical and mental status of the participants for determination of their care needs. Home-visit interviews were carried out between October and November 2004. The questionnaire asked about the background of the people in need of care, the awareness of the family caregiver of the adult guardianship law and the attitude of the caregiver toward the disclosure of a diagnosis of dementia. If the people in need of care were found to have dementia at the time of the questionnaire, a short memory questionnaire (SMQ; Koss *et al.*, 1993) was administered and the possibility of disclosure to the patient was investigated.

Statistical analysis

Pearson's correlation coefficients (r) were calculated for parametric data and Spearman's rank-order correlation coefficients (ρ) were calculated for non-parametric data. We used the χ^2 -test, the Kruskal–Wallis test and a one-way analysis of variance (ANOVA) for categorical comparisons of the data. Tukey's test was performed for multiple comparisons when the ANOVA showed a significant difference. Differences in the means of the SMQ among the groups were tested using the Student's t -test. A p -value of < 0.05 was considered to indicate statistical significance; all tests were two-tailed. All statistical analyses were performed on a personal computer with the statistical package SPSS 11.0 for Windows (SPSS, Inc., Chicago, IL, USA).

Results

Study 1

A total of 942 younger residents (47.1%) and 3273 (65.5%) older residents returned our questionnaire. Among the older residents, 173 were excluded because they were in hospital ($n = 53$), were residing in long-term care facilities ($n = 106$), had moved or died ($n = 5$), or the address of residence was unknown ($n = 9$). Characteristics of the respondents are shown in Table 1.

The perceptions of dementia by the respondents are shown in Table 2. Trends in answers are similar in younger and older participants. Approximately half of the participants answered that dementia is a morbid condition and more than 40% regarded dementia as a progressive disease. More than 10% of the respondents were not familiar with dementia as a disease.

Among the younger respondents, 34.1% ($n = 308$) said that they feared that they might develop dementia in the future, and 32.0% of the older

Table 1. Characteristics of responders in Study 1

	YOUNGER RESPONDENTS ($n = 942$)	OLDER RESPONDENTS ($n = 3100$)	<i>p</i> -VALUE
Gender			
Male	395 (42.3)	1403 (45.6)	< 0.042
Female	538 (57.7)	1673 (54.4)	
Age (years)			
40-49	306 (32.5)		
50-59	394 (41.9)		
60-64	241 (25.6)		
65-69		934 (30.3)	
70-79		1548 (50.3)	
80-89		541 (17.6)	
90+		57 (1.9)	
Certified care needs			
None		2548 (87.1)	
Need support		123 (4.2)	
Level 1		124 (4.2)	
Level 2		52 (1.8)	
Level 3		40 (1.4)	
Level 4		24 (0.8)	
Level 5		16 (0.5)	
Residency status			
Live by oneself	78 (8.6)	538 (20.6)	< 0.001
Live with spouse	199 (21.9)	282 (10.8)	
Other	633 (69.6)	1794 (68.6)	

Values are n (%).

Table 2. Perceptions of dementia among respondents

	YES	TEND TO YES	TEND TO NO	NO
Younger respondents				
Morbid condition	480 (67.9)	165 (23.3)	32 (4.5)	30 (4.2)
Disease of increasing frequency	466 (66.4)	181 (25.8)	35 (5.0)	20 (2.8)
Anyone may have dementia	441 (62.8)	163 (23.2)	53 (7.5)	45 (6.4)
Unfamiliar and scary disease	428 (48.0)	257 (28.8)	109 (12.2)	97 (10.9)
Familiar disease	302 (42.4)	280 (39.3)	86 (12.1)	44 (6.2)
Fatal disease	338 (38.9)	269 (30.9)	137 (15.7)	126 (14.5)
Disease unrecognized by society	303 (33.9)	360 (40.3)	129 (14.4)	102 (11.4)
Shameful disease	140 (15.7)	237 (26.7)	211 (23.7)	301 (33.9)
Untreatable disease	93 (10.4)	167 (18.7)	254 (28.4)	379 (42.4)
Older respondents				
Morbid condition	1528 (60.7)	659 (26.2)	194 (7.7)	135 (5.4)
Disease of increasing frequency	1387 (58.1)	775 (32.5)	218 (9.1)	8 (0.3)
Anyone may have dementia	1307 (50.5)	715 (27.6)	292 (11.3)	272 (10.5)
Unfamiliar and scary disease	1520 (60.5)	593 (23.6)	187 (7.4)	214 (8.5)
Familiar disease	1149 (44.9)	992 (38.8)	260 (10.2)	156 (6.1)
Fatal disease	978 (51.8)	631 (33.4)	275 (14.6)	5 (0.3)
Disease unrecognized by society	1112 (44.8)	832 (33.5)	250 (10.1)	290 (11.7)
Shameful disease	762 (31.2)	628 (25.7)	378 (15.5)	678 (27.7)
Untreatable disease	451 (18.1)	525 (21.0)	541 (21.7)	979 (39.2)

Values are *n* (%).

respondents ($n = 927$) had the same fear. Another 29.3% ($n = 265$) of younger and 28.3% ($n = 821$) of older respondents stated that they sometimes feared future dementia, while 28.1% ($n = 254$) of younger and 28.0% of older respondents ($n = 813$) rarely had this fear. Eight and a half percent ($n = 77$) of younger respondents and 11.7% of older respondents ($n = 339$) had no fear at all that they might have dementia in the future.

With regard to the adult guardianship law, 30.5% ($n = 271$) of younger respondents and 28.6% ($n = 797$) of older respondents knew about the law, but the majority of both younger ($n = 617$, 65.5%) and older respondents ($n = 1994$, 71.4%) did not know about it.

To a question assuming that the respondent would be afflicted with dementia in the future, 79.8% ($n = 710$) of younger respondents and 75.5% ($n = 2162$) of older respondents stated they would prefer to be told their diagnosis, while only 3.4% ($n = 30$) of younger respondents and 4.8% ($n = 138$) of older respondents do not wish to be told. The rest answered "don't know." The percentage of younger respondents who preferred disclosure was significantly higher than that of older respondents ($p = 0.025$); the reasons given for preferences regarding disclosure are shown in Table 3. Some of these reasons show a significant

Table 3. Disclosure of a diagnosis of dementia

REASONS WHY RESPONDENTS PREFER BE DISCLOSED A DIAGNOSIS OF DEMENTIA TO THEMSELVES	YOUNGER PEOPLE (<i>n</i> = 710)	OLDER PEOPLE (<i>n</i> = 2162)	<i>p</i> -VALUE
Because I have the right to know	199 (28.0)	633 (29.3)	0.279
Because I may want to consult or convey wills about the future	534 (75.2)	1292 (59.8)	< 0.001
Because telling the diagnosis would give me the option to receive treatment and rehabilitation	459 (64.6)	1297 (60.0)	0.015
Because I can accept the diagnosis and cope with problems positively	298 (42.0)	1005 (46.5)	0.020

REASONS WHY RESPONDENTS PREFER A DIAGNOSIS OF DEMENTIA NOT TO BE DISCLOSED TO THEMSELVES	YOUNGER PEOPLE (<i>n</i> = 30)	OLDER PEOPLE (<i>n</i> = 138)	<i>p</i> -VALUE
Because you cannot help having dementia when you grow old	17 (56.7)	49 (35.5)	0.004
Because there are no advantages in knowing the diagnosis due to reduced capacity for judgment	15 (50.0)	55 (39.9)	0.206
Because I may be depressed or lose hope by knowing it	21 (70.0)	58 (42.0)	0.275
Because knowing the diagnosis may exacerbate symptoms of dementia	4 (13.3)	30 (21.7)	0.219
Because it may be better untold as there is no effective remedy for reversing the condition	7 (23.3)	53 (38.4)	0.086

Values are *n* (%).

difference between younger and older respondents. However, in answer to a question assuming that a family member of the respondent has dementia, 85.1% (*n* = 749) of younger respondents and 82.5% (*n* = 2181) of older respondents stated that they would prefer that the patient be told his or her diagnosis, while only 4.7% (*n* = 41) of younger participants and 4.0% (*n* = 106) of older participants do not wish the patient to be told. The percentage of respondents who preferred telling the diagnosis of dementia to an affected family member did not differ significantly between younger and older respondents (*p* = 0.293).

The reasons given for preferences regarding the disclosure of a diagnosis of dementia to an affected family member are shown in Table 4; some of these

Table 4. Disclosure of a diagnosis of dementia to an affected family member

REASONS WHY RESPONDENTS PREFER DISCLOSURE OF A DIAGNOSIS OF DEMENTIA TO AN AFFECTED FAMILY MEMBER	YOUNGER RESPONDENTS (n = 749)	OLDER RESPONDENTS (n = 2252)	p-VALUE
Because he/she has the right to know	211 (28.2)	625 (27.8)	0.430
Because he/she may want to consult or convey wills about the future	612 (81.7)	1592 (70.7)	< 0.001
Because telling the diagnosis would give him/her the option to receive treatment and rehabilitation	535 (71.4)	1342 (59.6)	< 0.001
Because he/she can accept the diagnosis and cope with problems positively	259 (34.6)	849 (37.7)	0.068

REASONS WHY RESPONDENTS PREFER A DIAGNOSIS OF DEMENTIA NOT TO BE DISCLOSED TO AN AFFECTED FAMILY MEMBER	YOUNGER RESPONDENTS (N = 41)	OLDER RESPONDENTS (N = 113)	p-VALUE
Because he/she cannot help having dementia when he/she grows old	6 (14.6)	31 (27.4)	0.073
Because there are no advantages in knowing the diagnosis due to reduced capacity for judgment	17 (41.5)	40 (35.4)	0.307
Because he/she may be depressed or lose hope by knowing it	27 (65.9)	40 (35.4)	0.001
Because knowing the diagnosis may exacerbate symptoms of dementia	13 (31.7)	30 (26.5)	0.331
Because it may be better untold as there is no effective remedy for reversing the condition	11 (26.8)	53 (46.9)	0.019

Values are n (%).

reasons show a statistically significant difference between younger and older respondents.

Study 2

A total of 1444 (76.6%) family members of care recipients who were using some type of services provided by public long-term care insurance and 441 (21.4%) who did not use any service returned the questionnaire. Of the care recipients, 57.7% of the users of the care service and 53.9% of the

Table 5. Characteristics of responders in Study 2

	TOTAL <i>n</i> = 1885	WITHOUT DEMENTIA <i>n</i> = 1136 (60.2%)	WITH DEMENTIA <i>n</i> = 749 (39.8%)	<i>p</i> -VALUE
Gender (<i>n</i> = 1681, 89.2%)				
Male	617 (36.7)	371 (38.1)	246 (34.8)	0.098
Female	1064 (63.3)	604 (61.9)	460 (65.2)	
Age (years) (<i>n</i> = 1672, 88.7%)				
40–64	45 (2.7)	28 (2.9)	17 (2.4)	< 0.001
65–74	308 (18.4)	232 (23.8)	76 (10.9)	
75–84	713 (42.6)	435 (44.7)	278 (39.8)	
85+	606 (36.2)	278 (28.6)	328 (46.9)	
Residency (<i>n</i> = 1636, 86.8%)				
Live by oneself	118 (7.2)	76 (8.0)	42 (6.1)	< 0.001
Live with spouse	484 (29.6)	315 (33.2)	169 (24.6)	
Others	1034 (63.2)	559 (58.8)	475 (69.2)	
Certified level of care needs (<i>n</i> = 1678, 89.0%)				
Need support	1299 (77.4)	183 (18.7)	46 (6.6)	< 0.001
Level 1	445 (26.5)	319 (32.6)	126 (18.0)	
Level 2	341 (20.3)	193 (19.7)	148 (21.1)	
Level 3	290 (17.3)	119 (12.2)	171 (24.4)	
Level 4	222 (13.2)	8 (10.0)	24 (17.7)	
Level 5	151 (9.0)	66 (6.7)	85 (12.1)	
Duration in need of care (<i>n</i> = 1574, 83.5%)				
< 6 months	713 (45.3)	109 (12.1)	604 (89.3)	< 0.001
6 months–3 years	422 (26.8)	393 (43.8)	29 (4.3)	
> 3 years	439 (27.9)	396 (44.1)	43 (6.4)	

Values are *n* (%).

non-users were female. The percentage of people with dementia was significantly higher in the care service users (43.3%, *n* = 625) than in non-users (28.1%, *n* = 124) ($p < 0.001$). Combining the users and non-users of care service, there were significant differences with regard to age ($p < 0.001$), residency status ($p < 0.001$), certified levels of care needs ($p < 0.001$) and duration in need of care ($p < 0.001$) between the care recipients with and those without dementia (Table 5).

In the case of a diagnosis of dementia, after the exclusion of the respondents who answered “don’t know,” 79.0% (*n* = 650/823) of family members of care recipients without dementia and 58.4% (*n* = 301/515) of family members of care

Table 6. Preferences of disclosure of a diagnosis of dementia

REASONS WHY FAMILY MEMBERS OF A CARE RECIPIENT PREFER DISCLOSURE OF A DIAGNOSIS OF DEMENTIA	WITHOUT DEMENTIA (<i>n</i> = 650)	WITH DEMENTIA (<i>n</i> = 301)
Because he/she has the right to know	208 (32.5)	99 (32.9)
Because he/she may want to consult or convey wills about the future	476 (74.4)	216 (71.8)
Because telling the diagnosis would give him/her the option to receive treatment and rehabilitation	412 (64.4)	175 (58.1)
Because he/she can accept the diagnosis and cope with problems positively	347 (54.2)	156 (51.8)
Because I feel guilty about not telling the truth	136 (21.3)	52 (17.3)
Others	14 (2.2)	14 (4.7)

REASONS WHY FAMILY MEMBERS OF A CARE RECIPIENT PREFER NO DISCLOSURE OF A DIAGNOSIS OF DEMENTIA	WITHOUT DEMENTIA (<i>N</i> = 173)	WITH DEMENTIA (<i>N</i> = 214)
Because he/she cannot help having dementia when he/she grows old	56 (32.4)	119 (55.6)
Because there are no advantages in knowing the diagnosis due to reduced capacity for judgment	87 (50.3)	146 (68.2)
Because he/she may be depressed or lose hope by knowing it	73 (42.2)	48 (22.4)
Because knowing the diagnosis may exacerbate symptoms of dementia	44 (25.4)	42 (19.6)
Because it may be better untold as there is no effective remedy for reversing the condition	58 (33.5)	62 (29.0)
Others	14 (8.1)	14 (6.5)

Values are *n* (%).

recipients with dementia said that they would prefer to tell the afflicted person of the diagnosis, while 21.0% (*n* = 173/823) of the family members of the care recipients without dementia and 41.6% (*n* = 214/515) with dementia preferred not to disclose the diagnosis. There was a significant difference in the percentages of family members who wanted to disclose the diagnosis between those whose care recipient did not have dementia at the time of the questionnaire and those whose care recipient had already been diagnosed with dementia ($p < 0.001$). The reasons for preferring to disclose the diagnosis are shown in Table 6. Male family members of care recipients were significantly more likely to prefer disclosure than female family members (male 73.4%, female 68.6%, $p = 0.048$). The spouses were significantly more likely to want their care recipients to be told the diagnosis than non-spouse caregivers (74.9% vs. 66.6%, respectively, $p = 0.002$). The certified level of long-term care needs had no significant effect on disclosure preference ($p = 0.121$), nor did residence status (living alone or

living with family) ($p = 0.282$). The mean SMQ score of care recipients whose family preferred disclosure (17.6 ± 5.6 S.D.) and that of patients whose family did not prefer disclosure (17.0 ± 5.4 S.D.) did not differ significantly ($t = 1.256$, $p = 0.210$).

Of the patients whose family preferred disclosure of the diagnosis of dementia, after the exclusion of 26 patients who had not confirmed whether they were told the diagnosis or not, 62.5% (172/275) were told the diagnosis by their physicians, and 37.5% (103/275) were not told. Of the patients whose family preferred no disclosure to the patient, 64.3% (128/199) were told the diagnosis by their physicians, and 35.7% (71/199) were not told, after the exclusion of 15 patients who had not confirmed whether they were told the diagnosis or not.

Discussion

The present survey reveals that the residents of an urban area of Japan strongly favor the disclosure of a hypothetical diagnosis of dementia (Study 1), with 85.1% of younger respondents and 82.5% of older respondents expressing positive attitudes toward disclosure to their family members. In 1996, Maguire *et al.* reported that in a memory clinic in Ireland, only 17% of family members wanted disclosure to the patient of a diagnosis of dementia. This disagreement might be attributed to cultural differences. The fact that we found a willingness to disclose a diagnosis of dementia to a family member in this study population is also in contrast to the somewhat negative attitude toward disclosing a diagnosis of cancer in Japan (Elwyn *et al.*, 2002), while the trend is the opposite in western countries (Holroyd *et al.*, 2002), where people might be more sensitive to losing autonomy or human dignity by having dementia. The favorable attitudes toward diagnosis disclosure of dementia in the current study were, however, in agreement with two recent reports from western countries (Holroyd *et al.*, 2002; Pinner and Bouman, 2003) and one from Taiwan (Lin *et al.*, 2005). This may suggest that the increased public awareness of dementia in recent years has affected attitudes toward this issue irrespective of cultural differences. One recent survey performed in an island in Okinawa in Japan reported 29.9% of the caregivers were positive for disclosure (Sugiyama *et al.*, 2003), whereas another survey in an urban area in Japan showed that 71% of caregivers were in favor of disclosure (Yamashita *et al.*, 2002), which is comparable to our current results. These inconsistent results within the same county may be due to the different areas of the surveys. The attitudes in a relatively rural area in Japan might be shifting toward a more positive outlook with an increase in public awareness, but further investigation is necessary.

In the present study, the older people were less favorable to disclosure of their own hypothetical diagnosis, but no difference was found between younger and older respondents in terms of preference of disclosure of a hypothetical diagnosis to an affected family member. Although the reasons why the younger people were more favorable to disclosure of their own hypothetical diagnosis were unclear, they may have more interest in their own condition.

There was a significant difference regarding the disclosure of diagnosis between younger and older respondents in the general population and an even more striking difference between the two caregiver groups whose recipients either had or did not have dementia. Our results show that the older adults were less eager to be told of their own diagnosis and that the caregivers of patients with dementia were also less eager to tell their patients. In general, older people are more likely to have had personal experiences related to dementia than younger people, and caregivers of patients with dementia may have broader experience and knowledge of dementia, which might give them an understanding of the deeper implications of disclosure. With this deeper understanding of dementia based on actual personal experiences, caregivers of patients with dementia may become paternalistic or reluctant to deal with the potential grief reaction of a family member, and therefore may be reluctant to disclose the diagnosis. Indeed, in a study in the U.S.A., Turnbull *et al.* (2003) found that people who had had personal experience with Alzheimer's disease (AD) were less likely to want to know themselves if they had AD than those without personal experience. In the case of patients with advanced dementia, advance planning including disclosure may have less significance. As expected, we found less favorable attitudes toward the disclosure in caregivers (Study 2) than in non-caregivers (Study 1). Although the difference in study design (questionnaires sent by mail *vs.* interview-based questionnaires) makes a direct comparison difficult, similar reasons to those given above may explain the relative reluctance of the caregivers to disclose the diagnosis of dementia.

A study conducted at a Dutch memory clinic reported that spouses were significantly more likely to want their care recipients to be told the diagnosis than non-spouse caregivers (Dautzenberg *et al.*, 2003), which is consistent with the present results.

Fahy *et al.* (2003) found that lower scores on the Mini-mental State Examination of a care recipient was a predictor of the desire of the caregivers for the diagnosis to remain undisclosed in a study performed at a U.K. clinic. In the present study, however, the mean SMQ score, which reflects the severity of dementia (Koss *et al.*, 1993), was not significantly different between the two different preference groups for disclosure, although it was slightly lower in the group that did not prefer disclosure.

Some studies, including one from Japan (Johnson *et al.*, 2000; Maguire *et al.*, 1996; Yamashita *et al.*, 2002), have found a double standard toward disclosure in that many people may have a more favorable attitude toward disclosure to themselves than toward disclosure to others. We did not find this trend in the present study; this may reflect changes in the attitudes of Japanese society after the introduction of long-term care insurance, which has promoted the socialization of care.

While one study reported that disclosure of diagnosis to patients and family members is beneficial (Smith and Beattie, 2001), another report revealed that about half of family members studied experienced a poor reaction from an informed patient (Holroyd *et al.*, 2002), and possible consequences even include some catastrophic reactions such as suicide of the patient (Rohde *et al.*, 1995). Thus, in order to obtain a social consensus, this issue requires careful substantiation.

The new guardianship law for adults has been in effect in Japan since 2000. The law protects persons with dementia with respect to their autonomy, and the right to know or not to know one's own disease is one of the basic human rights granted within this autonomy. The present study showed strongly positive attitudes toward disclosure of a diagnosis of dementia in Japanese society; however, only about 30% of the participants knew of the new guardianship system. Low dissemination of the system may be due to poor publication to the possible beneficiaries.

Because our survey was conducted in an urban area, it is not known whether these results are representative of the whole of Japan, including residents in rural areas, and this is a major limitation of the study.

In summary, the present survey of caregivers and non-caregivers in an urban city of Japan has demonstrated that the desire for disclosure of a diagnosis of dementia is relatively high. National debate on this issue is required.

Conflict of interest

None.

Description of authors' roles

H. Umegaki designed the study and wrote the paper. J. Ohnishi was responsible for the statistical design of the study and carried out the statistical analysis. Y. Suzuki, H. Endo and A. Iguchi helped to write the paper.

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