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Table 1. Clinical Profiles of 3,177 Japanese

	Men	Women
Number of Subjects	1245	1932
Age	46.7 ± 12.3	48.5 ± 12.6
Height (cm)	168.7 ± 6.0	155.8 ± 5.7
Weight (kg)	71.1 ± 11.7	56.1 ± 9.0
Waist Circumference (cm)	85.3 ± 9.8	73.7 ± 9.6
Hip circumference (cm)	94.5 ± 6.2	91.2 ± 6.1
SBP (mmHg)	130.0 ± 15.8	124.2 ± 17.5
DBP (mmHg)	81.3 ± 11.2	76.3 ± 10.3
Triglyceride (mg/dl)	147.0 ± 117.5	97.5 ± 69.7
HDL cholesterol(mg/dl)	54.9 ± 14.8	66.8 ± 16.6
Blood sugar(mg/dl)	105.8 ± 28.3	96.3 ± 20.2

Mean ± SD
SBP: Systolic blood pressure
DBP: Diastolic blood pressure

Cigarette smoking

The data on cigarette smoking was obtained at interviews by well-trained staff in a structured way. The subjects were asked if they currently smoked cigarettes. When the answer was "yes", they were classified as current smokers and further questions were asked regarding the average number (pieces) of cigarette smoked per day and their age at starting smoking. When the answer was "no", further questions were asked if they had ever smoked continuously. When the answer was "no", they were classified as non-smokers and the answer was "yes", they were classified as previous smokers.

Based on answers to those questions, the cumulative amount of cigarette consumption was expressed as the Brinkman Index (BI: number of cigarette consumed per day multiplied by years of smoking) (9) and the current smokers were classified into 2 groups of BI: BI<600, BI≧600, respectively.

Anthropometric measurements

The anthropometric parameters were evaluated by using the following respective parameters such as height, body weight, waist circumference, hip circumference. The waist circumference was measured at the umbilical level and the hip was measured at the widest circumference over the trochanter in standing subjects after normal expiration (10).

Blood pressure measurements

Blood pressure of each participant was measured after resting at least 15 minutes in the sitting position.

Blood sampling and assays

We measured overnight fasting serum levels of high density lipoprotein (HDL) cholesterol, triglycerides (L Type Wako Triglyceride · H, Wako Chemical, Osaka) and plasma glucose. The atherogenic index was calculated as follows: (total cholesterol-HDL cholesterol) /HDL cholesterol.

Diagnosis of metabolic syndrome

The syndrome was defined (2), among men with a waist circumference in excess of 85 cm and women with a waist circumference in excess of 90 cm (11), as having 2 or more components from among the following: 1) Dyslipidemia: triglyceride≧150 mg/dl and/or HDL cholesterol<40 mg/dl, 2) Hypertension: blood pressure≧130/85 mmHg, 3) Impaired glucose tolerance: fasting plasma glucose≧110 mg/dl.

Statistical analysis

Data are expressed as mean ± standard deviation (SD) values. Relationship between metabolic syndrome and cigarette smoking was tested using χ^2-test and logistic regression analysis. Effect of metabolic syndrome and cigarette smoking on atherogenic index was analyzed by ANOVA and Scheffe's F test: $p<0.05$ was considered to be statistically significant.

Results

Four hundred and forty men (35.3%) and 142 women (7.4%) were classified as current smoker (Table 2). The prevalence of current smoker gradually decreased with age in both sexes.

We clarified the prevalence of metabolic syndrome (Table 3). Among 3,177 Japanese subjects, 614 men (49.3%) had a waist circumference in excess of 85 cm and 126 women (6.5%) had a waist circumference exceeding 90 cm. In addition, the prevalence of metabolic syndrome gradually increased with age under the age of 70 and 334 men (26.8%) were diagnosed as having metabolic syndrome. In turn, the prevalence of metabolic syndrome in women gradually increased with age, especially over the age of 50, and only 69 women (3.6%) were diagnosed with metabolic syndrome.

We evaluated the relationship between metabolic syndrome and cigarette smoking (Table 4). The prevalence of metabolic syndrome was closely linked to cigarette smoking in men. The prevalence of current smoker with metabolic syndrome (41.0%) was significantly higher than that with non-metabolic syndrome (33.3%) with and without adjustment of age in men. However, such a relationship was not observed in women. To investigate the effect of metabolic syndrome and cigarette smoking on atherogenic index, we compared atherogenic index among four groups [metabolic syndrome (-) cigarette smoking (-): MS(-)CS(-), metabolic syndrome (-) cigarette smoking (+): MS(-)CS(+), metabolic syndrome (+) cigarette smoking (-): MS(+)CS(-), metabolic syndrome (+) cigarette smoking (+): MS(+)CS(+)] (Table 5). In men, the atherogenic index in subjects with MS(+)CS(+) was significantly higher than in the other three groups and the effect of metabolic syndrome and cigarette smoking on atherogenic index was noted. In women, the atherogenic index in subjects with MS(+)CS(-) was significantly higher than that in subjects with MS(-)CS(-) and MS(-)CS(+) and the effect of cigarette smoking on atherogenic index was not revealed.

To investigate the effect of number of cigarettes consumed per day and cumulative amount of cigarette consumption on metabolic syndrome in men, we evaluated the prevalence of metabolic syndrome in men with current ciga-

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Table 2. Prevalence of Cigarette Smokers as Classified into Age Groups

Age	Number of subjects	Current smoker	Non somker	Previous somker
Men				
20-29	114	52 (45.6)	48 (42.1)	14 (12.3)
30-39	269	109 (40.5)	106 (39.4)	54 (20.1)
40-49	353	144 (40.8)	127 (36.0)	82 (23.2)
50-59	300	99 (33.0)	114 (38.0)	87 (29.0)
60-69	170	31(18.2)	78 (45.9)	61 (35.9)
70-79	39	5 (12.8)	15 (38.5)	19 (48.7)
Total	1245	440 (35.3)	488 (39.2)	317 (25.5)
Women				
20-29	197	45 (22.8)	148 (75.1)	4 (2.0)
30-39	264	29 (11.0)	226 (85.6)	9 (3.4)
40-49	499	36 (7.2)	453 (90.8)	10 (2.0)
50-59	571	24 (4.2)	542 (94.9)	5 (0.9)
60-69	333	8 (2.4)	321 (96.4)	4 (1.2)
70-79	68	0 (0.0)	66 (97.1)	2 (2.9)
Total	1932	142 (7.4)	1756 (90.9)	34 (1.8)

( ): percentage of subjects as classified into age groups

Table 3. Prevalence of Metabolic Syndrome as Classified into Age Groups

Age	Number of subjects	Waist circumference ≧85cm (Men) ≧90cm (Women)	Blood pressure SBP≧130mmHg and/or DBP≧85mmHg	Impaired glucose tolerance Blood sugar≧110mg/dl	Dyslipidemia Triglyceride≧150mg/dl and/or HDL cholesterol<40mg/dl	Metabolic syndrome
Men						
20-29	114	32 (28.1)	40 (35.1)	10 (8.8)	29 (25.4)	13 (11.4)
30-39	269	116 (43.0)	122 (45.4)	32 (11.9)	125 (46.5)	45 (16.7)
40-49	353	199 (56.4)	210 (59.5)	72 (20.4)	188 (53.3)	113 (32.0)
50-59	300	163 (54.3)	198 (66.0)	107 (35.7)	139 (46.3)	93 (31.0)
60-69	170	90 (52.9)	125 (73.5)	64 (37.6)	99 (58.2)	61 (35.9)
70-79	39	14 (35.9)	31 (79.5)	11 (28.2)	15 (38.5)	9 (23.1)
Total	1245	614 (49.3)	726 (58.3)	296 (23.8)	595 (47.8)	334 (26.8)
Women						
20-29	197	4 (2.0)	18 (9.1)	2 (1.0)	32 (16.2)	1 (0.5)
30-39	264	12 (4.5)	44 (16.7)	11 (4.2)	62 (23.5)	5 (1.9)
40-49	499	28 (5.6)	155 (31.0)	29 (5.8)	115 (23.0)	10 (2.0)
50-59	571	39 (6.8)	293 (51.3)	67 (11.7)	217 (38.0)	25 (4.4)
60-69	333	29 (8.7)	220 (66.1)	57 (17.1)	169 (50.8)	17 (5.1)
70-79	68	14 (20.6)	60 (88.2)	22 (32.4)	47 (69.1)	11 (16.2)
Total	1932	126 (6.5)	790 (40.9)	188 (9.7)	642 (33.2)	69 (3.6)

( ): percentage of subjects as classified into age groups
SBP: Systolic blood pressure
DBP: Diastolic blood pressure

Table 4. Relationship between Metabolic Syndrome and Cigarette Smoking

	Men		Women	
	MS(−)	MS(+)	MS(−)	MS(+)
Current smoker	303	137	137	5
Non smoker	383	105	1694	62
Previous smoker	225	92	32	2
		ab		

a: $P<0.01$ by χ^2-test
b: $P<0.01$ after adjusting for age by logistic regression analysis
MS: metabolic syndrome

Table 5. Effect of Metabolic Syndrome and Cigarette Smoking on Atherogenic Index

	MS(−)CS(−)	MS(−)CS(+)		MS(+)CS(−)		MS(+)CS(+)	
Men	2.7 ± 1.0	2.9 ± 1.2	a	3.5 ± 1.1	ab	4.1 ± 1.3	abc
Women	2.3 ± 1.0	2.3 ± 1.0		3.2 ± 1.1	ab	3.1 ± 1.0	

a: $P<0.01$ vs MS(−)CS(−)
b: $P<0.01$ vs MS(−)CS(+)
c: $P<0.01$ vs MS(+)CS(−)
MS: Metabolic syndrome
CS: Cigarette smoking

rette smoking (Tables 6, 7). The number of cigarettes consumed per day was closely linked to the metabolic syndrome and the prevalence of metabolic syndrome in men with Brinkman index≧600 (39.8%) was significantly higher than that in men with Brinkman index<600 (25.1%) with and without adjustment for age.

Discussion

The present study is the first report showing that the relationship between metabolic syndrome, defined by the new criterion of metabolic syndrome in Japan, and cigarette smoking. Metabolic syndrome has important clinical and public health implications because it is a common disorder in Japan (2, 3). Previous studies documented that the metabolic syndrome is important risk factor for diabetes, coronary heart disease and stroke (12-14). Our study shows new and important information about the relationship between the metabolic syndrome and cigarette smoking in a large sample of Japanese population.

We revealed the prevalence of metabolic syndrome in both sexes in Japan as we previously reported (3). In addition, sex difference in the prevalence of metabolic syndrome was noted from our study. This was due to the fact that the prevalence of women with a waist circumference in excess of 90 cm was significantly lower than that of men with a

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Table 6. Prevalence of Metabolic Syndrome as Classified into Age and Cigarette Smoking Groups in Men

	Current smoker (number of cigarette)			Non smoker	Previous smoker	
Age	1-19/day	20-39/day	40-/day			
20-29	2(15.4)	5(15.6)	2(15.4)	4(8.3)	0(0.0)	
30-29	2(7.1)	16(23.9)	4(28.6)	15(14.2)	8(14.8)	
40-49	15(42.9)	31(34.8)	8(40.0)	32(25.2)	27(32.9)	
50-59	4(22.2)	28(47.5)	8(36.4)	25(21.9)	28(32.2)	
60-69	5(38.5)	6(37.5)	0(0.0)	28(35.9)	22(36.1)	
70-79	0(0.0)	1(100.0)	0(0.0)	1(6.7)	7(36.8)	
Total	28(25.2)	87(33.0)	22(33.8)	105(21.5)	92(29.0)	a b

( ): percentage of subjects as classified into age groups
a: $P<0.01$ by χ^2-test
b: $P<0.01$ after adjusting for age by logistic regression analysis

Table 7. Relationship between Metabolic Syndrome and Brinkman Index in Men with Current Cigarette Smoking

	MS(−)	MS(+)
Brinkman index<600	194	65
Brinkman index≧600	109	72
		ab

a: $P<0.01$ by χ^2-test
b: $P<0.01$ after adjusting for age by logistic regression analysis
MS: metabolic syndrome

waist circumference exceeding 85 cm. We could not explore whether metabolic syndrome is closely linked to future cardiovascular disease or the importance of sex differences. Follow-up studies are required to demonstrate such links.

The prevalence of current smoker in Japan was reported to be 46.8% in men and 11.3% in women by the National Nutrition Survey in Japan (7); our results were not similar and the prevalence of current smoker was less than that in the previous study. The enrolled subjects in our study were undertaking annual health check-ups and they might be more careful of their own health compared to the subjects in the National Nutrition Survey.

Smokers have abnormalities in lipoprotein metabolism (15) and endothelial function (16). Moreover, there is some evidence that smokers are at greater risk than nonsmokers of becoming insulin resistant and have hyperinsulinemia (17, 18). Nakanishi et al investigated the relationship between metabolic syndrome by using the modified National Cholesterol Education Program definition (NCEP) and cigarette smoking in 3,649 middle-aged Japanese male office workers (19). Ishizaka et al reported, by also using the modified NCEP definition, the association between metabolic syndrome and cigarette smoking in 5,033 Japanese, and that metabolic syndrome was an independent risk factor for carotid plaque (20). In the present study, we compared atherogenic index in subjects with and without metabolic syndrome, also with and without cigarette smoking. The effect of metabolic syndrome and cigarette smoking on atherogenic index was noted in men. Therefore, metabolic syndrome and cigarette smoking were considered to be important risk factors for atherosclerosis. In addition, the number of cigarettes smoked per day and the Brinkman index were also closely linked to metabolic syndrome. Based on these findings, smoking is closely associated with the prevalence of metabolic syndrome in men.

Potential limitations still remain in our study. The cross-sectional study design in our study makes it difficult to infer causality between metabolic syndrome and cigarette smoking. Sex difference was noted in the relationship between metabolic syndrome and cigarette smoking. We previously reported that there was discrepancy in the prevalence of metabolic syndrome between new criterion in Japan and NCEP definition (3) and the prevalence of metabolic syndrome in this study was only 3.6% in women. In addition, the prevalence of current smoker in women was also lower than that in the National Nutrition Survey. Although cigarette smoking was noted as a risk factor for atherosclerosis in both sexes (21), the association between metabolic syndrome by using the new criterion in Japan and cigarette smoking was noted in men, but not in women in this study. Therefore, our findings are applicable to clinical and public health practice settings. In conclusion, cigarette smoking is closely linked to metabolic syndrome in the Japanese population. Further intervention studies are necessary to test the effect of prevention and treatment of metabolic syndrome.

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Systemic Tumor Embolism Mimicking Gefitinib ('IRESSA')-induced Interstitial Lung Disease in a Patient with Lung Cancer

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□ CASE REPORT □

Systemic Tumor Embolism Mimicking Gefitinib ('IRESSA')-induced Interstitial Lung Disease in a Patient with Lung Cancer

Shigeki UMEMURA, Daizo KISHINO*, Masahiro TABATA, Katsuyuki KIURA, Katsuyuki HOTTA, Kenji NISHII*, Yasushi TANIMOTO, Arihiko KANEHIRO, Kenji NOTOHARA**, Hiroshi UEOKA and Mitsune TANIMOTO

Abstract

We describe a 55-year-old man with advanced adenocarcinoma of the lung who received gefitinib ('IRESSA'). After gefitinib administration for 7 months, computed tomography scan of the chest demonstrated diffuse ground glass opacity and he was suspected to have developed gefitinib-induced interstitial lung disease (ILD). However, transbronchial lung biopsy (TBLB) revealed tumor cells in the middle-size lung vessels. Afterwards, multiple infarctions of the brain, spleen and left kidney were detected. Then, he was considered to have developed systemic tumor emboli, a rare complication. The clinical presentation of this patient was difficult to discriminate from that of ILD, and TBLB was useful in the differential diagnosis.
(Internal Medicine 44: 979–982, 2005)

Key words: NSCLC, tumor embolism, gefitinib, ground glass opacity, transbronchial lung biopsy

Introduction

Gefitinib ('IRESSA') is an orally active inhibitor of epidermal growth factor receptor tyrosine kinase (EGFR-TKI) (1). In phase I and II clinical trials, gefitinib exhibited antitumor activity for advanced non-small cell lung cancer (NSCLC) (2–4). As well as 'gefitinib-induced interstitial lung disease' (ILD), severe pulmonary toxicity has been observed in patients receiving gefitinib (5–8). In Japan, the incidence of gefitinib-induced ILD has been reported to be about 4% (5, 6), with approximately one-third of the cases being fatal (7), although in the rest of the world the incidence is only around 0.3%.

Systemic tumor embolism, particularly pulmonary embolism which leads to life-threatening respiratory insufficiency, is an extremely rare complication of malignancies. The majority of cases of systemic tumor embolism reported in the literature have developed in patients with bronchogenic carcinoma (9–15), either intraoperatively or early in the postoperative period (10, 12, 13). We report a patient with systemic tumor embolism, in whom transbronchial lung biopsy (TBLB) proved useful in determining a tumor embolism and not gefitinib-induced ILD.

Case Report

A 55-year-old man complaining of exertional dyspnea was admitted to our hospital in January 2001. Massive right pleural effusion was detected by a chest radiograph and cytological examination of pleural effusion showed adenocarcinoma cells. The patient was diagnosed with adenocarcinoma of the lung and assessed to have stage IV disease (T4N3M1), with multiple bone metastases.

The patient received four cycles of a triplet chemotherapy regimen consisting of cisplatin (60 mg/m^2) and docetaxel (60 mg/m^2) administered on day 1, and irinotecan (50 mg/m^2) on day 2, repeated every 3 weeks. He achieved a partial response lasting for 12 months but was readmitted in March 2002 due to regrowth of the primary lesion and a mediastinal lymph node. He received six cycles of vinorelbine (25 mg/m^2) administered on days 1 and 8, repeated every 3 weeks.

From the Department of Hematology, Oncology and Respiratory Medicine Okayama University Graduate School of Medicine and Dentistry, Okayama, *the Department of Pulmonary Medicine, Okayama Institute of Health and Science, Okayama and **the Department of Pathology, Okayama University Graduate School of Medicine and Dentistry, Okayama

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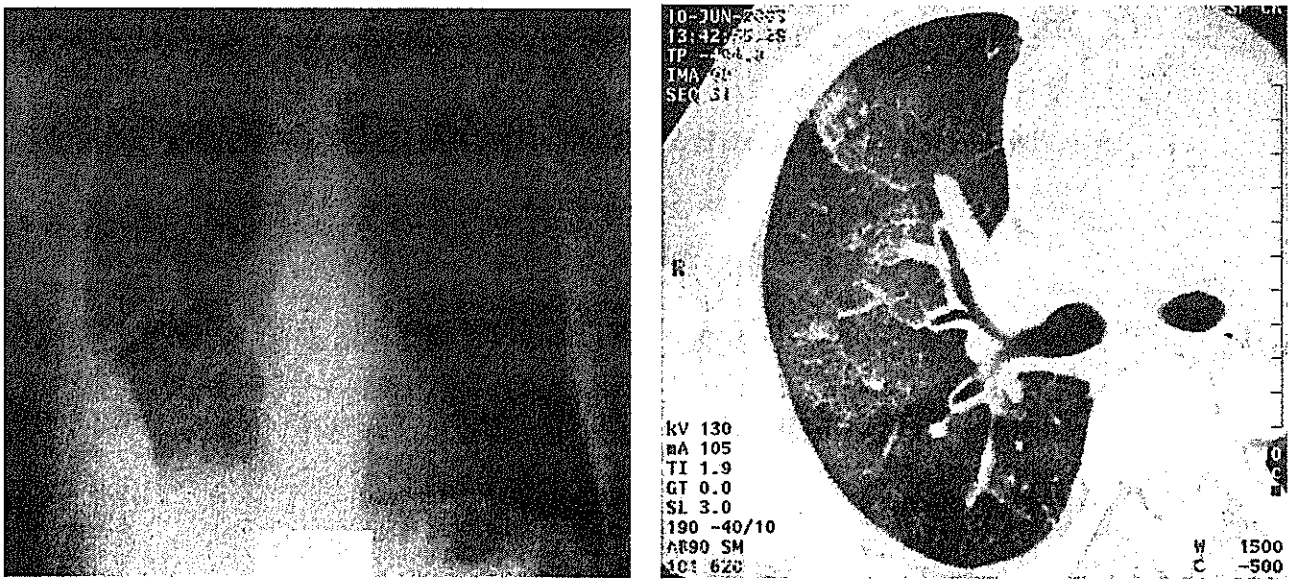
Reprint requests should be addressed to Dr. Shigeki Umemura, the Department of Hematology, Oncology and Respiratory Medicine Okayama University Graduate School of Medicine and Dentistry, 2-5-1 Shikata-cho, Okayama 700-8558



A B

Figure 1. Chest radiograph (A) and CT scan (B) showing ground glass opacity in the right middle to lower fields.

However, this treatment was not effective and gefitinib (250 mg orally once daily) was started in September 2002, which resulted in a partial response lasting for 7 months.

On May 5, 2003, the patient was readmitted due to elevation of tumor markers although he was asymptomatic on admission. Chest radiograph and computed tomography (CT) scans of the chest demonstrated new ground glass opacities in the right middle and lower lung field (Fig. 1). Breath sound was weak in the right middle and lower chest, and at this point, gefitinib was discontinued. Results of laboratory examination on admission are listed in Table 1; anemia, thrombocytopenia and hypoxia were observed. Serum levels of lactate dehydrogenase, C-reactive protein, fibrin-degradation product and D-dimers were elevated, as were serum levels of the two tumor markers, carcinoembryonic antigen (CEA) and sialyl Lewis X antigen (SLX). Bleeding from the right upper lobe bronchus was observed by fiberoptic bronchoscopy. TBLB was performed from the right upper (B^3a) bronchus. Histologically, small foci of adenocarcinoma cells were present within middle-size lung vessels (Fig. 2). The patient suddenly developed a sensory loss of the left hand and blindness on June 7, 2003. Magnetic resonance imaging (MRI) of the brain clearly demonstrated multiple cerebral infarctions (Fig. 3). Considering the clinical course and the pathological findings of the TBLB samples, the tumor cell emboli in the cerebral arteries were considered to be the cause of multiple cerebral infarctions. Furthermore, abdominal CT scans revealed low density areas in the spleen and left kidney (Fig. 4), which were compatible with infarction by systemic tumor cell emboli.

The patient was treated with a combination of carboplatin (250 mg/m^2) and paclitaxel (180 mg/m^2), but no response was observed. One month later, he died of tumor progression.

Table 1. Laboratory Data on Admission

Complete Blood Count	UN 12 mg/dl
WBC 5,300/μl	Cr 1.17 mg/dl
Nt 77%	Na 142 mEq/*l*
Mo 7%	K 3.7 mEq/*l*
Eo 2%	Cl 111 mEq/*l*
Ba 0%	Ca 7.9 mg/dl
Ly 14%	FBS 105 mg/dl
Hb 11.1 g/dl	CRP 2.2 mg/dl
RBC 358×10^4/μl	**Tumor marker**
Ht 33.8%	CEA 17.9 ng/ml
Plt 7.9×10^4/μl	Cyfra 9.2 ng/ml
Coagulation	SLX 99.3 U/ml
PT 14.4 sec	ProGRP 22.8 pg/ml
APTT 32.9 sec	NSE 4.9 ng/ml
FDP 148.0 μg/ml	**Arterial Blood Gas (room air)**
D-dimer 21.79 μg/ml	pH 7.491
Biochemical Examination	PaO_2 54.8 mmHg
T.bil 0.9 mg/dl	$PaCO_2$ 30.2 mmHg
Alp 363 IU/*l*	BE −0.2 mEq/*l*
γ-GTP 29IU/*l*	SaO_2 86.9%
AST 29 IU/*l*	**Urinalysis**
ALT 15 IU/*l*	Pro (−)
TP 6.8 g/dl	Glu (−)
Alb 4.2 g/dl	Occult blood (+)
LDH 318 IU/*l*	

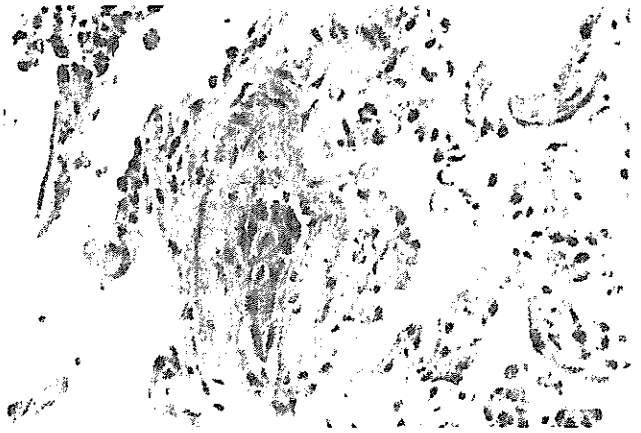
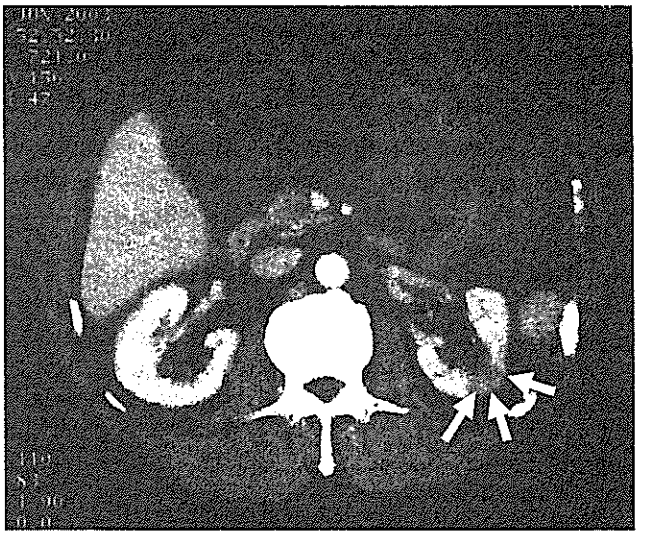


Figure 2. Transbronchial lung biopsy showing small foci of adenocarcinoma within middle-size lung vessels (HE stain, ×200).



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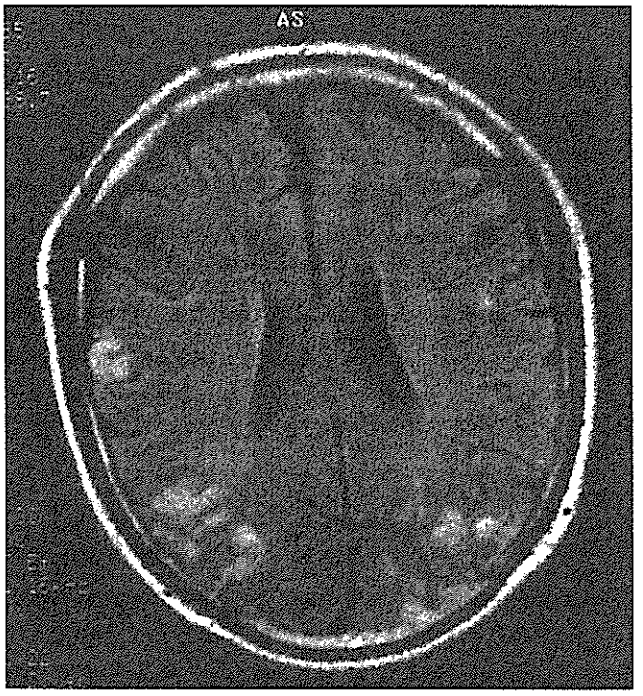
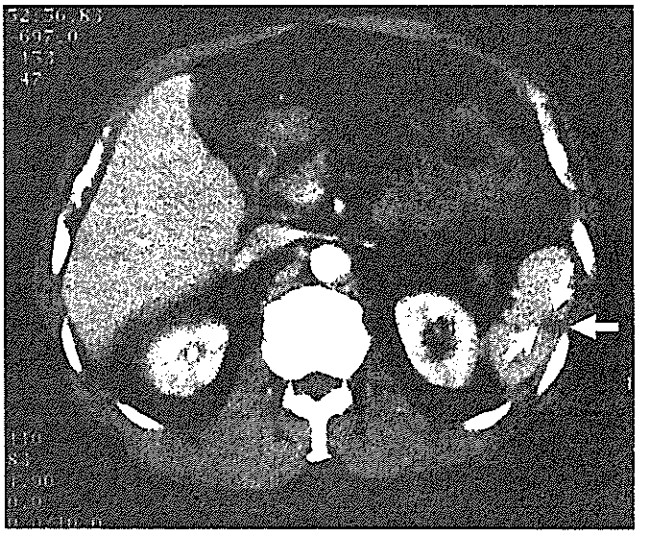


Figure 3. Brain MRI demonstrating multiple cerebral infarction.



B

Figure 4. Abdominal CT revealing a low density area of the left kidney (A) and a low density area of the spleen (B).

Discussion

A definitive diagnosis of abnormal pulmonary shadow on a chest radiograph in patients with lung cancer is complicated by the potential for numerous causes in this setting, including pre-existing chronic lung disease, respiratory tract infections, drug-induced pulmonary disease and disease progression. ILD has been reported frequently in patients with lung cancer receiving gefitinib (5–8). Although the median time to onset of gefitinib-induced ILD was reported to be 24 days in Japan and 42 days in the U.S., there was a rare case developing ILD at seven months after gefitinib administration (7). Whenever gefitinib-induced ILD is suspected, treatment with gefitinib should be terminated. However, since all cases reported as gefitinib-induced ILD were not histopathologically confirmed, it is likely that gefitinib is discontinued inappropriately in a substantial number of patients in whom ground glass opacity is attributable to causes other than gefitinib.

Tumor embolism in middle-size lung vessels has been rarely diagnosed by TBLB to date. In the previous reports

describing systemic tumor embolism, the majority of cases have occurred in patients with left-sided atrial myxomas (16). To the best of our knowledge, fewer than 70 cases of non-myxomatous tumor emboli have been reported. The majority of non-myxomatous tumor emboli are presumed to originate from pulmonary neoplasms (9–15), and tumor emboli originating from lung cancer in cerebral, coronary and mesenteric circulation, aorta, and extremity vessels have been previously reported (17). It is considered likely that lung cancer cells erode and partially occlude one or more of the pulmonary veins, and tumor cells are ejected into the systemic circulation after tumor mass fractures. In the current case, the origin of the embolus was histologically proven to be lung cancer that had invaded middle-sized pulmonary arteries. Tumor cells seemed to have affinity to vessels in the brain, kidney and spleen.

The clinical presentation of tumor embolism in lung vessels is very similar to that of gefitinib-induced ILD. The characteristic images of gefitinib-induced ILD are diffuse ground-glass opacities (5–8). Tumor embolism in middle-size lung vessels is considered to be one of the 'small-vessel diseases'. In the context of 'small-vessel diseases', ground-glass opacity is also most frequently observed, which may reflect relative overperfusion or diffuse pulmonary hemorrhage, because there is thickening of the interstitium and partial filling of the airspaces with blood (18). Although radiological findings of drug-induced pneumonitis were often bilateral (19), several cases showing laterality of the shadows like the current case were reported (20). Although the clinical presentation of systemic tumor embolism in this patient was difficult to discriminate from that of gefitinib-induced ILD, TBLB proved to be very useful for etiologic diagnosis of ground glass opacities in lung fields.

The current case demonstrates that when an abnormal shadow is identified on a chest radiograph or CT scan of a patient receiving gefitinib for management of lung cancer, TBLB can prove useful for the differential diagnosis of ILD.

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原著

住民を対象とした胸部CT検診での胸膜プラークの検討

西井研治[*1]、正影三恵子[*1]、久本晃子[*1]、守谷欣明[*1]、玄馬顕一[*2]、岸本卓巳[*2]、堀田勝幸[*3]、瀧川奈義夫[*3]、田端雅弘[*3]、木浦勝行[*3]、谷本光音[*3]

和文要旨

わが国でも悪性中皮腫の増加が認められ、職域検診とあわせて住民検診でも石綿曝露者の把握が重要になっている。しかし、住民検診受診者に石綿による変化がどの程度あるのか、あるいはそれをどの程度指摘できるのかは明らかでない。そこで今回、CT住民検診対象者中の石綿（アスベスト）による胸膜肥厚斑（以下胸膜プラーク）の頻度と検出率について検討した。対象は2000年に岡山県西部のK市住民に対して行った胸部CT検診受診者621人（男性592人、女性29人）で、胸部X-PとCT検診フィルムをアスベスト検討委員会で再読影し、胸膜肥厚所見を詳細に検討した。621人のうち石綿による胸膜肥厚は14例で受診者の2.3%（男性では2.4%）に認められた。そのうち胸部X-PでもプラークがCT指摘できたのは6例で1.0%（同1.0%）であった。8例についてはCTでのみ指摘でき、両法による検出率には2.3倍の開きがあり、アスベスト対策においても胸部CT検診の有用性が示唆された。

キーワード：　胸部CT検診、アスベスト、胸膜肥厚斑、プラーク

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はじめに

悪性胸膜中皮腫は、わが国では比較的まれな疾患といわれていたが、過去のわが国のアスベストの多量の使用が原因で今後徐々に増加し、2000年から2029年までの30年間に58,000人の死亡が予想されると報告されている[1]。中皮種の大半は過去の石綿（アスベスト）曝露により生じると考えられており[2]、わが国で大きな社会問題になっている。中皮腫の発生部位は胸膜が90%近くを占めており、胸部X-Pで発見されることが多い。また、胸膜肥厚斑（以下胸膜プラーク）が石綿曝露をあらわし、しかも胸膜中皮腫の危険指標になることから[3]、胸部検診でプラークを指摘することは重要である。ただし、石綿使用から中皮腫や肺癌発生までに20年以上、平均40年かかるといわれており、職域検診のみではfollow upは困難で、退職後はかなりの数の石綿曝露者が住民検診を受診することになると思われる。一方で、住民検診受診者に石綿による変化がどの程度あるのか、あるいはそれをどの程度指摘できるのかは明らかでない。そこで今回、CT住民検診対象者中の石綿（アスベスト）によるプラークの頻度と検出率について検討した。

[*1]岡山県健康づくり財団附属病院
（〒700-0952　岡山県岡山市平田408-1）
e-mail: nkenji@okakenko.jp
[*2]岡山労災病院呼吸器内科
[*3]岡山大学医学部血液・腫瘍・呼吸器内科

対象と方法

今回研究対象としたK市は、大きな工場や産業はなく、第一次産業が市の主産業であるような自治体であり、特にアスベスト関連産業はないが、製鉄所をもつ工場地帯が隣接し

た市に存在している。対象者は 2000 年に K 市で行った胸部 CT 検診受診者である。胸部 CT 検診受診者は 621 人（男性 592 人、女性 29 人）で男性が大半であるが、現喫煙者および過去喫煙者を条件としたためにこのような偏りがでた。年齢分布は 60-69 歳が 302 人と最も多く、ついで 70 以上が 208 人であった。

胸部 CT の撮影条件は、深吸気での 1 回の呼吸停止中に連続的に撮影することを原則とし、撮影範囲は肺尖部から横隔膜下まで肺野のすべてが入るように設定した。X 線管回転速度は 1 回転 1.9 秒以下とし、X 線ビーム幅は 1 cm、テーブル移動速度は X 線管 1 回転あたり 2 cm とし、撮影条件は 120kV、X 線管電流は 50mA/sec 1 回転とした。

胸部 CT は 2 枚のフィルムに焼き付け、条件は WL;-600～-700　WW;1500～2000 とした。

胸部 X-P と CT 検診フィルムをアスベスト検討委員会で再読影し、胸膜肥厚所見を詳細に検討し、プラークの検出率を算定した。読影方法は合議によった。なおアスベスト検討委員会は、岡山労災病院副院長を委員長に内科 3 名、放射線科 2 名の石綿肺の専門家で構成された委員会である。CT および胸部 X-P は全例再読影した。

プラークは胸部 X-P 上、face-on（レントゲン正面）あるいは in-profile（レントゲン接線方向）で指摘できた。face-on での特徴的な陰影を呈するものの指摘は比較的容易であったが、in-profile では筋肉による陰影や胸膜外脂肪組織との鑑別が難しい場合があった。

一方胸部 CT では限局性、平板状で平滑あるいは結節状の胸膜肥厚として見られ、石灰化を伴わなくても CT 値はやや高く、筋層ないしそれ以上であることをめやすに判断した。

あわせて K 市住民の通常検診受診者 8339 名と岡山県南部の造船が主産業の T 市の間接 X-P フィルムの再読影もおこない、プラークの比率についても検討した。

結果

胸部 CT 検診を受診した 621 人のうち、発見された肺癌は 5 例で発見率は 10 万人対 805.2 であった。この 5 例には 1 例も石綿肺およびプラークは認められなかった。621 人のうち胸膜肥厚所見を認めたものは 43 例で、そのうち石綿による胸膜変化が強く疑われるものが 14 例（33%）であった（Table 1）。

Table 1. Characteristics of patients with pleural thickening recognized by chest CT

No. of patients	43
Male/female	43/0
Mean age (range)	69 (49-75)
Asbestos plaque/others	14/29

残り 29 例は結核性あるいは非特異的な炎症によるものが考えられた。Table 2 にプラークを認めた 14 例の臨床的特徴を示すが、全例男性で平均年齢は 71.5 歳で重喫煙者が多かった。プラークの有所見率は受診者の 2.3%（男性では 2.4%）であった。14 例のうち胸部 X-P でプラークを指摘できるものは 6 例で 1.0%（同 1.0%）であった。8 例については CT でのみ指摘でき、両法による検出率に

Table 2. Characteristics of patients with pleural plaques

No. of patients	14
Male/female	14/0
Mean age (range)	71.5 (58-75)
Mean smoking index (range)	664.6 (120-1100)
Detected on chest X-P (yes/no)	6/8

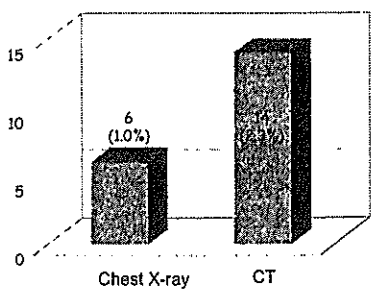

Figure 1. No. of patients with pleural plaques detected by chest X-ray or CT

は2.3倍の開きがあった（Fig 1）。CT検診を受診しなかった間接X-Pによる通常検診を受けたK市住民のプラークの有所見率は男性で1.1%とCT検診受診者の直接X-Pの有所見率と同様であった。参考のため、造船所があるT市でのプラークの有所見率も求めたが、男性で8.5%と高い値を示した（Fig. 2）。

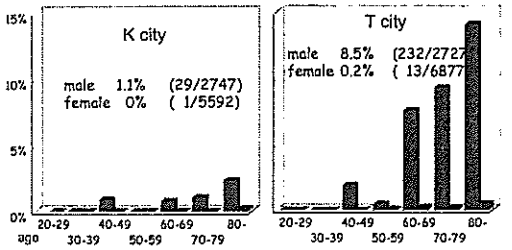

Figure 2. Incidence of pleural plaques detected by chest indirect X-ray based on ages in K city and T city

今回のCT検診でプラークを指摘した14例のうち石綿曝露の職業歴を有するものは10例（71%）であった。具体的には溶接工2例、製鉄所勤務2例、建築業3例などであった。残り4例については追跡調査でもアスベスト関連業種とのかかわりは認められなかった。14例のうち石綿肺は1例も認めなかった。5年間、追跡を行っているが、プラークを有する14例に悪性胸膜中皮腫や肺癌の発生は見られていない。

考察

石綿曝露と胸膜中皮腫の関連は1950年代にドイツから報告され、職業性曝露者の胸部検診は積極的に行われてきた。また直接アスベストをあつかう労働者ではなく、その衣服を取り扱う家族（傍職業性家庭内曝露）や、工場の近くで遊んでいた子供や石綿鉱山の近くに住んでいた人たちへの被害（近隣曝露）についても報告されている[4]。わが国でも熊本県での鉱山近隣居住者へのプラークの多発[5]や石綿工場近くに住んでいた主婦の中皮腫例が報告されて、今後、一般住民にアスベスト健康被害が発生する可能性が危惧されている[6][7]。しかし、わが国の住民にしめる石綿曝露者の正確な比率は明らかではなく、その発見方法についても議論されたことはない。このような状況から、肺癌を対象として行われている胸部CT検診で指摘できるプラークの検討は重要であると考えられる。

従来、われわれは住民の石綿曝露の指標として、間接X-Pでの比率を使ってきたが、今回のCT検診受診者の検討から、実際の曝露の比率はその2.4倍程度はあることがわかった。胸部CTのプラーク検出力は、岡山労災病院で実施しているアスベスト健診受診者136名の検討をみると、胸部X-Pによる検出率19.1%にくらべ胸部CT（通常撮影条件）による検出率は49.3%と2.6倍になっており[8]、われわれの行った低線量検診モードでも同程度の検出能力があることが明らかになった。

ただ、胸部CTでプラーク所見がなければアスベストの曝露がないとは言えない。胸部CT所見と病理学的所見を比較した報告はないが、Wainらの胸部X-Pと剖検肺の検討では胸部X-Pで指摘できたのは28%に過ぎず[9]、われわれの成績を当てはめてみると胸部CTでも実際の曝露者の70%程度しか指摘できていないのではないかと考えられる。

いずれにしても精度の高いアスベスト検診を実施し、中皮腫や肺癌のスクリーニングに役立てるためには、従来の胸部X-P検診では不十分で、胸部CTを用いた検診がぜひ必要である。

K市でのプラークの比率が多いのか少ないのかは、全県的な調査が行われていないため判断は困難である。われわれが行っている住民検診のうち、もっともプラーク所見が多いT市の間接X-Pのプラーク所見率は8.5%（男性）で、この地区でCT検診を実施したとすると、16%程度はプラーク所見が認められると考えられる。T市の男性人口が約33,000人であるから、数千人のアスベスト曝露者がいることになる。このような地域での胸部CT検診の必要性は高く、今後検討していきたい。

プラークを認めた14例の職歴を今回詳しく調べたが、一般的にアスベスト職種としてよく知られている溶接工や製鉄、建築業以外に、肥料工場、セメント工場、紡績工場などでも石綿曝露が起こっていることが明らかとなった。わが国では非常に多くの製品にアスベストが使用され、使用者や作業従事者がそ

れを認知せずにいることは非常に問題であり、今後、あらゆる機会を通じで情報を提供していく必要がある。また、4名はまったく石綿関連職歴がなく、環境曝露が否定できないが、過去の居住歴などさらに調査が必要である。

今後、各地で行われている住民を対象とした胸部CT検診での同様な検討が、当学会を中心に行われることを期待したい。

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Pleural plaques detected by lung cancer screening with low-dose spiral CT

Kenji Nishii[1], Mieko Masakage[1], Akiko Hisamoto[1], Yoshiaki Moritani[1], Kenichi Gemba[2], Takumi Kishimoto[2], Katsuyuki Hotta[3], Nagio Takigawa[3], Masahiro Tabata[3], Katsuyuki Kiura[3], and Mitsune Tanimoto[3]

Okayama Health Foundation Hospital[1],
Respiratory Disease Center for Workers, Okayama Rousai Hospital[2]
Department of Internal Medicine II, Okayama University Medical School[3]

The incidence of malignant mesothelioma related to asbestos exposure is increasing in Japan. It is important to know the prevalence of pleural diseases by environmental asbestos-exposure among the residents in addition to workers in asbestos-related occupations. Pleural plaques are considered the significant radiographical findings of exposure to asbestos. However, the prevalence of pleural plaques in Japanese residents remains unclear. This study was undertaken to assess the prevalence of pleural plaques detected by CT screening, which was performed for 621 residents (592 male and 29 female) in K city, western part of Okayama Prefecture on 2000. Fourteen of 621 (2.3%) had pleural plaques detected by CT, however, only 6 (1.0%) could be found by chest X-ray. The prevalence of pleural plaques detected by chest CT screening was 2.3 times compared to prevalence detected by chest X-ray screening. CT screening assists in detecting pleural plaques.

Key words: Thoracic CT screening, Asbestos, Asbestos plaque
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RESEARCH COMMUNICATION

5-Year Survival Rates for Primary Cancer Sites at Cancer-Treatment-Oriented Hospitals in Japan

Naoyuki Okamoto[1*], Nobuhiro Saruki[2], Haruo Mikami[3], Kousuke Yamashita[4], Yoichi Maruyama[5], Tokujiro Yano[6], Yuka Imamura[7], Satoshi Kaneko[7,8], Hideo Tanaka[9], and the Survival Study Group of Japanese Association of Clinical Cancer Centers

Abstract

In Japan, The Japanese Association of Clinical Cancer Centers (JACCCs) was established in 1965 by systematizing cancer-treatment-oriented hospitals. The core center of JACCCs is the National Cancer Center in Tokyo. In 1984, JACCCs created The "Improvement for Clinical Cancer Centers in Japan" Study Group (The Study Group) which has subsequently routinely evaluated the effectiveness of the therapy that is provided. In general, the 5-year (relative) survival rate is employed as an indicator of the treatment efficacy. The present survey used the PC software program KAP developed by Chiba Cancer Center in Japan, to calculate 5-year observed survival rates and the 5-year relative survival rates using Ederer II methods. The overall 5-year relative survival rates in patients with stomach (15,353 patients), colon (5,054), rectum (3,695), lung (10,153), breast (11,302) and cervix of the uterus (6,336) were 68.7%, 72.2%, 69.4%, 28.1%, 86.1% and 81.1%, respectively. The survival rates discussed so far are principally observed survival rates. The 5-year relative survival rate for those institutions that specialize in cancer treatment should become an index for Japanese cancer treatment.

Key Words: Cancer-treatment-oriented hospital - 5 year relative survival rate - stomach cancer - colon cancer - rectal cancer - lung cancer - breast cancer - cervical cancer

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Introduction

In Japan, The Japanese Association of Clinical Cancer Centers (JACCCs) was established in 1965 by systematizing some cancer-treatment-oriented hospitals. The core center of JACCCs is the National Cancer Center in Tokyo. As of 31 March 2004, a total of 30 institutes throughout Japan belonged to the JACCCs. Eight of these cancer centers are supported by the National Government, while the others are supported by local prefectural governments or by a private foundation. Executive board members of JACCCs evaluate cancer centers for suitability, prior to allowing membership.

In 1984, JACCCs created The "Improvement for Clinical Cancer Centers in Japan" Study Group (The Study Group) which has subsequently, routinely evaluated the effectiveness of the treatment that is provided. In general, the 5-year (relative) survival rate is used as an indicator of the effectiveness of cancer treatments (Esteve et al., 1994). The Study Group uses the method of cumulative survival analysis (Cutler & Ederer, 1958) for its calculations. Frequently in clinical medicine, this indicator is calculated in relation to each cancer site within the body so that a comparison can be made between different stages of cancer or between different treatments (for example surgery, chemotherapy or radiation therapy) for each site (Watanabe et al., 1995).

There are two key aspects that are of interest when examining the effectiveness of cancer treatment. Firstly it is important to demonstrate that 5-year survival rates in Japan have risen from past to present so as to attain a true evaluation of the progress of cancer treatment in this country. This requires information to be collected on a nationwide basis. Secondly, it is useful to make comparisons between survival rates at different hospitals. This is especially relevant today because there is increasing concern among the Japanese

*1 Kanagawa Cancer Center, Division of Cancer Prevention and Cancer Control, 2 Gunma Cancer Center, Dept. of Anesthesia, 3 Chiba Cancer Center, Dept. of Epidemiology, 4 Kanagawa Cancer Center, Division of Radiation Therapy, 5 Niigata Cancer Center, Dept. of Anesthesia, 6 Saga Prefectural Hospital KOSEIKAN, Dept. of Surgery, 7 National Cancer Center, Statistics and Cancer Control Division, 8 Nagasaki University, Inst. of Tropical Medicine, 9 Osaka Medical Center for Cancer and Cardiovascular Diseases, Dept. of Cancer Control and Statistics *For Correspondence: Division of Cancer Prevention and Cancer Control, Kanagawa Cancer Center, 1-1-2 Nakao, Asahiku, Yokohama 241-0815, Japan Fax: +81-45-366-3157 e-mail: okamoto@gancen.asahi.yokohama.jp*

public about the differences in cancer survival rates between teaching hospitals and general hospitals.

In this paper, we examine the 5-year (relative) cancer survivals in patients who were admitted to JACCCs between 1988 and 1992. The purpose of this study is to obtain base-line site and stage specific 5-year (relative) survival rates from these JACCCs. The data will help clarify the current situation and contribute to the continued monitoring of cancer treatment at these institutions in Japan.

Materials and Methods

In 1996, the Study Group embarked on a survey to collect data on cancer patients who had been treated at JACCCs seven years beforehand, in order to calculate relative survival rates. This survey collected data over a period of 5 years, from 1996 to 2000. This survey collected data relating to in-patient primary cases of cancer of the stomach (ICD9-No. 151), colon (153), rectum (154), lung/trachea (162), breast (174), and cervix of the uterus (180), where treatment had taken place during a 5-year period from January 1, 1988 to December 31, 1992. The data collected included the following: 1) patient number, 2) gender, 3) date of birth (or age at time of diagnosis), 4) date of confirmed diagnosis, 5) primary site (ICD9-No.), 6) clinical stage, 7) survival confirmation date, and 8) survival status (alive or dead). The stage was classified in accordance with the current guidelines of each relevant academic society, at 1988-1992 of the data under medical treatment period (Japanese Research Society for Gastric Cancer, 1985; Japanese Society for Cancer of the Colon and Rectum, 1988; The Japanese Lung Cancer Society, 1989; The Japanese Breast Cancer Society, 1989; Japanese Society of Obstetrics and Gynecology, 1988).

It was the aim of the survey to include patient follow-up that took place more than 5 years after treatment. In view of this, this survey considered the data of any patient, who underwent follow-up in under 1825-days, to be censored. The expected survival rate, which was used in the calculation of the relative survival rate, was based on the Japanese life expectancy used by the Survey Department of the National Cancer Center in its own studies (Arimoto, 1985). The relative survival rate was calculated based on the following formula:

$$\text{Relative survival rate} = \frac{\text{Observed survival rate}}{\text{Expected survival rate}} \times 100$$

This survey used the PC software program KAP to

Table 1. The Number of Collected Cancers by Major Site

Institution	Years of admission	Stomach (151)	Colon (153)	Rectum (154)	Lung (162)	Breast (174)	Cervix (180)	Total
Cancer Center Group (CCG)	-	8,154	2,409	1,914	5,394	7,466	4,013	29,350
1. Miyagi Cancer Center	1989-92	451	118	82	254	117	68	1,090
2. Tochigi Cancer Center	1988-92	578	158	146	419	292	112	1,705
3. Gunma Cancer Center	1988-92	369	108	111	326	333	314	1,561
4. Saitama Cancer Center	1988-92	1,007	196	223	795	976	641	3,838
5. Chiba Cancer Center	1988-92	607	180	107	283	422	332	1,931
6. National Cancer Center	1988-92	1,281	448	389	968	1,136	381	4,603
7. The Cancer Institute Hospital	1988-90	833	220	141	245	1,263	336	3,038
8. Kanagawa Cancer Center	1988-92	834	258	175	682	671	617	3,237
9. Aichi Cancer Center	1988-92	1,056	381	259	657	1,037	541	3,931
10. Shikoku Cancer Center	1988-92	783	158	184	333	617	490	2,565
11. Kyushu Cancer Center	1990-92	355	184	97	432	602	181	1,851
Cancer Center with General Hospital (WGH)	-	2,254	647	522	1,895	1,790	815	7,923
12. Hokkaido Cancer Center	1988-92	326	115	102	508	702	406	2,159
13. Ibaragi Prefectural Center Hospital	1991-92	105	44	31	36	37	7	260
14. Niigata Cancer Center	1988-92	1,284	285	239	1,002	805	298	3,913
15. National Kure Medical Center	1988-92	539	203	150	349	246	104	1,591
Hospitals Specialized in Geriatric Diseases (SGD)	-	4,230	1,499	968	2,232	1,663	1,166	11,758
16. Yamagata Medical Center for Cancer & LRD*1	1988-92	1,257	376	299	340	234	127	2,633
17. Fukui Medical Center for Geriatric Diseases	1988-92	1,496	441	284	274	308	114	2,917
18. Shiga Medical Center for Geriatric Diseases	1991	79	42	26	50	43	32	272
19. Osaka Medical Center for Cancer & CVD*2	1988-92	802	463	236	801	603	405	3,310
20. Hyogo Medical Center for Geriatric Diseases	1988-92	596	177	123	767	475	488	2,626
Regional Teaching Hospitals (RTH)	-	715	499	291	632	383	342	2,862
21. Aomori Prefectural Central Hospital	1990-92	288	124	79	301	73	46	911
22. Iwate Prefectural Central Hospital	1990-92	109	163	111	110	73	120	686
23. Nagoya Medical Center	1991-92	172	97	33	72	108	107	589
24. Yamaguchi Grand Medical Center	1990-92	146	115	68	149	129	69	676
Total	-	15,353	5,054	3,695	10,153	11,302	6,336	51,893

*1: LRD; Life-related Diseases, *2: CVD; Cardiovascular diseases

Table 2. Numbers and Percentages of Cancers by Site and Stage

Site (ICD No.)	Stage (%)												Total (%)	
	I		II		III		IV		V		unknown			
Stomach (151)	6,938	(45.2)	1,353	(8.8)	2,025	(13.2)	2,518	(16.4)	-	(-)	2,519	(16.4)	15,353	(100.0)
Colon (153)	1,166	(23.1)	801	(15.8)	793	(15.7)	552	(10.9)	395	(7.8)	1,347	(26.7)	5,054	(100.0)
Rectum (154)	911	(24.7)	587	(15.9)	616	(16.7)	387	(10.5)	235	(6.4)	959	(26.0)	3,695	(100.0)
Lung (162)	2,282	(22.5)	513	(5.1)	4,180	(41.2)	1,086	(10.7)	-	(-)	2,092	(20.6)	10,153	(100.0)
Breast (174)	3,784	(33.5)	4,412	(39.0)	1,180	(10.4)	329	(2.9)	-	(-)	1,597	(14.1)	11,302	(100.0)
Cervix (180)	2,340	(36.9)	1,004	(15.8)	789	(12.5)	240	(3.8)	-	(-)	1,963	(31.0)	6,336	(100.0)
Total	17,421	(33.6)	8,670	(16.7)	9,583	(18.5)	5,112	(9.9)	630	(1.2)	10,477	(20.2)	51,893	(100.0)

calculate 5-year observed survival rates and the 5-year relative survival rates using Ederer II methods (Esteve, 1994). KAP was developed by the Chiba Cancer Center in Japan and is based on the Kaplan-Meier Method (Kaplan and Meier, 1958).

Results

Table 1 shows the institutions that co-operated with this survey. This survey covered 11 institutions that specialized in cancer treatment (referred to as CCG), 4 institutions that specialized in cancer treatment working together with a general hospital (WGH), 5 institutions specializing in geriatric diseases (SGD) and 4 institutions affiliated with regional teaching hospitals (RTH).

The total number of annual discharges from these institutions, over the 5 years from 1988 until 1992, was about 450,000 and cancer patients accounted for about 200,000 (44.4%) of this total (Okamoto, 2004). Some 24 (90.5%) of the 27 institutions cooperated in providing patient information. Patient information without the patient's name and address was collected for 51,893 cases (Table 1). This figure was broken down by site as follows: the stomach was the most affected site with 15,353 cases (29.6%), followed by the breast with 11,302 cases (21.8%), the lungs with 10,153 cases (19.6%), the cervix of the uterus with 6,336 (12.2%), the colon with 5,054 cases (9.7%) and the rectum with 3,695 cases (7.1%).

The data, which was collected by site classification, was then further classified by clinical stage, as shown in Table 2. It was not possible to determine the stage for 10,477 cases (20.2%), a very high proportion. The number of censored cases was 4,698 (9.0%).

Table 3-1 shows the observed survival rate and Table 3-2 shows the relative survival rate by primary site and by stage. The overall 5-year relative survival rates in patients with stomach, colon, rectum, lung, breast and cervix of the uterus were 68.7%, 72.2%, 69.4%, 28.1%, 86.1% and 81.1%, respectively (Table 3-2). For the stomach, the 5-year relative survival rates by stage were 98.0% for Stage I, 80.9% for Stage II, 51.5% for Stage III and 9.6% for Stage IV. Very similar trends were observed in the 5-year relative survival rate by stage for the colon, the rectum, the breast and the cervix of the uterus. However, different results were obtained for cancer of the lung, with the overall 5-year relative survival rate, a very low 28.1%. In addition, for lung cancer, there was an apparently greater difference in relative survival rates between stages than was observed in the other primary sites (67.1% for Stage I, 39.7% for Stage II, 15.0% for Stage III, 4.2% for Stage IV).

Table 3-1. Five-year Crude Survival Rates (%) and Standard Error by the Site and by the Stage

Site (ICD No.)	Stage (%)												Total (%)	
	I		II		III		IV		V		unknown			
Stomach (151)	89.1	(0.00)	73.2	(0.03)	46.9	(0.06)	8.7	(0.45)	-	(-)	47.8	(0.04)	62.3	(0.00)
Colon (153)	87.7	(0.01)	79.2	(0.03)	68.0	(0.06)	36.0	(0.36)	11.4	(2.07)	63.4	(0.04)	65.4	(0.01)
Rectum (154)	87.5	(0.02)	76.5	(0.06)	64.4	(0.10)	35.1	(0.50)	13.6	(2.77)	55.7	(0.09)	63.4	(0.02)
Lung (162)	62.4	(0.03)	35.6	(0.37)	13.5	(0.18)	3.9	(1.74)	-	(-)	17.8	(0.23)	25.2	(0.03)
Breast (174)	94.4	(0.00)	87.7	(0.00)	66.7	(0.04)	24.4	(1.02)	-	(-)	70.5	(0.03)	83.5	(0.00)
Cervix (180)	92.4	(0.00)	67.6	(0.01)	45.5	(0.16)	15.7	(2.42)	-	(-)	88.3	(001)	78.4	(0.00)

Table 3-2. Five-year Relative Survival Rates (%) and Standard Errors by the Site and Stage

Site (ICD No.)	Stage (%)												Total (%)	
	I		II		III		IV		V		unknown			
Stomach (151)	98.1	(0.00)	80.9	(0.03)	51.5	(0.06)	9.6	(0.05)	-	(-)	53.4	(0.05)	68.7	(0.00)
Colon (153)	96.5	(0.01)	89.4	(0.04)	74.7	(0.07)	41.8	(0.34)	12.5	(2.27)	69.6	(0.05)	72.2	(0.01)
Rectum (154)	95.8	(0.02)	84.9	(0.06)	70.7	(0.11)	38.1	(0.54)	14.2	(2.88)	60.2	(0.09)	69.4	(0.02)
Lung (162)	67.1	(0.04)	39.7	(0.04)	15.0	(0.20)	4.2	(1.88)	-	(-)	19.9	(0.26)	28.1	(0.03)
Breast (174)	97.2	(0.00)	90.5	(0.00)	69.0	(0.05)	25.5	(1.06)	-	(-)	72.9	(0.03)	86.1	(0.00)
Cervix (180)	94.7	(0.00)	71.8	(0.05)	49.2	(0.11)	17.8	(2.74)	-	(-)	90.4	(0.00)	81.1	(0.00)

Discussion

The ultimate objective of all cancer strategies is to eliminate deaths from cancer, which in reality is close to impossible. However, by investigating the effectiveness of both the medical care itself and the associated activities of this medical care, cancer prevention and treatment measures can be significantly improved. The calculation of 5-year or 10-year (relative) survival rates plays an important role in measuring effectiveness and thus achieving this objective. However it is difficult to find statistics that enable easy comparisons. To start with, relative survival cancer statistics are not available in Japan at the national level. Some information has been collated from the site-specific registries that are run by academic societies in Japan (Watanabe et al., 1995). However, studies only calculate the observed survival rate and omit to calculate the relative survival rate. Another problem is that the study periods used in the survival calculations differ from study to study and therefore vary across primary sites of the cancer. This causes difficulty in determining survival rates that relate to a particular period.

In this discussion, stomach cancer is used as a representative primary site for discussion purposes because of the stomach cancer leading in cause of death in Japan. The survey found the 5-year observed survival rate for this site to be 62.3% and the relative survival rate to be 68.8%. This observed survival rate is consistent with the 5-year observed survival rate of 57.8% for patients (in whom cancer had been diagnosed from 1979 through 1982) reported by one of the site-specific registries in Japan (The Japanese Research Society for Gastric Cancer, 1995). Another study conducted by the Osaka Medical Center for Cancer and Cardiovascular Diseases, determined this survival rate to be 68.1% (relative) for in-patients (1987-1990), using the hospital cancer registry data (Tanaka, 1997).

The survival rates discussed so far are principally observed survival rates. They are calculated, in many cases, without any regard for the composition of gender, age or earliness of detection rate of the targeted patient group. It is thus difficult to compare survival rates geographically or chronologically between target groups that differ in terms of gender, age or earliness of detection rate. Even if the survival rates are calculated taking into account gender and age, another major problem arises. It is often unclear whether the calculation includes patients who died from causes other than the cancer in question. Furthermore, if the survival rate is calculated considering gender and age, in many cases the number of subjects drops dramatically, making it difficult to obtain a reliable survival rate. The relative survival rate is thus a way of eliminating these comparison problems. (Parkin, 1991).

The results of this study on JACCCs were calculated from data that contained a relatively high percentage of censored cases (9%). It is important to note that the higher rate of censored cases in this study is likely to overestimate survival, especially for patients with a less favorable prognosis.

The Study Group plans to accurately track and tabulate the relative survival rate annually and, as of 2005, they are in the process of defining guidelines for the standardization of data collection, data processing, and publication of survival rates. With these guidelines in mind, the Study Group aims to collect reliable data from participating institutions and monitor cancer survivals in future. The 5-year relative survival rate for these institutions that specialize in cancer treatment will become an index for Japanese cancer treatment.

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ORIGINAL ARTICLE

Reiko Numazaki · Etsuko Miyagi · Ryo Onose
Tsuneo Nakazawa · Ken Sugiura · Kunio Asukai
Hiroki Nakayama · Atsushi Miyamatsu
Naoyuki Okamoto · Fumiki Hirahara

Historical control study of paclitaxel–carboplatin (TJ) versus conventional platinum-based chemotherapy (CAP) for epithelial ovarian cancer

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Abstract
Background. As the first-line chemotherapy for epithelial ovarian cancer, the paclitaxel–carboplatin (TJ) regimen has replaced the cyclophosphamide, epirubicin, and cisplatin or carboplatin (CAP) regimen in our institutes since 1998. Both regimens were retrospectively compared for effectiveness and safety to verify the adequacy of the TJ regimen.
Methods. Women with epithelial ovarian cancer at FIGO stage Ic – IV were enrolled into the study and were assigned to either the CAP group (57 cases, from 1991 until 1998) or the TJ group (49 cases, from 1998 until 2002). The response rate, progression-free survival (PFS), and overall survival (OS) were compared in both groups. Adverse effects were also evaluated.
Results. The TJ group received an average of 6.3 courses of paclitaxel at 170.6 mg/m^2 and carboplatin with an AUC of 4.3, while the CAP group received 5.8 courses of cisplatin at 61.4 mg/m^2. The response rates were 82.8% in the TJ group and 70.6% in the CAP group at stage III–IV. The median OS was 43.9 months in the TJ group and 44.3 months in the CAP group. There was no statistically significant difference in effectiveness between the two groups. Peripheral neuropathy, myalgia/arthralgia, and allergic reactions were found significantly more often in the TJ group, but every adverse effect occurring in the TJ group was clinically controllable. In contrast, renal dysfunction occurred more frequently in the CAP group.
Conclusion. This study demonstrated that the TJ regimen is as effective as the CAP regimen in its antitumor effect for epithelial ovarian cancer, and has controllable adverse effects.

Key words Carboplatin · Cisplatin · Chemotherapy · Ovarian cancer · Paclitaxel

R. Numazaki · E. Miyagi (✉) · R. Onose · T. Nakazawa · K. Sugiura · F. Hirahara
Department of Obstetrics and Gynecology, Yokohama City University School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan
Tel. +81-45-787-2691; Fax +81-45-701-3536
e-mail: emiyagi@med.yokohama-cu.ac.jp

K. Asukai
Department of Obstetrics and Gynecology, Yokohama Minami-Kyosai Hospital, Yokohama, Japan

H. Nakayama
Department of Gynecology, Kanagawa Cancer Center, Yokohama, Japan

A. Miyamatsu · N. Okamoto
Department of Epidemiology, Kanagawa Cancer Center Research Institute, Yokohama, Japan

Introduction

As chemotherapy for epithelial ovarian cancer, the cisplatin-based cyclophosphamide and cisplatin (CP) or cyclophosphamide, adriamycin or its derivatives, and cisplatin (CAP) regimens have shown some treatment efficacy from the 1980s through the first half of the 1990s. However, the GOG111 Study reported that a combination of paclitaxel and cisplatin, known as the TP regimen, was superior to the conventional CP regimen in response rates, median survival, and progression-free survival (PFS) time.[1] Since that study was published, the TP regimen had been regarded as the first-line chemotherapy for ovarian cancer. The report by Piccart et al.,[2] representing a European and Canadian collaborative research group, confirmed this treatment regimen's superiority, leading to the establishment of the regimen as the latest standard for epithelial ovarian cancer chemotherapy. Later, large-scale comparative trails, such as GOG 158[3] and OVAR-3[4] by the AGO group, were carried out to evaluate a possible reduction in the TP regimen neurotoxicity by replacing cisplatin with carboplatin. Those interim reports, suggesting that the combination therapy including carboplatin reduced peripheral neuropathy while maintaining the equivalent effectiveness, led to the generalization of the current paclitaxel and carboplatin (TJ) regimen as the first-line chemotherapy. Although the TJ regimen has been commonly used in Japan since paclitaxel was approved in 1997, it has remained unclear how effective