— Original Article —

Frequency of examinations for cancer among patients with lifestyle-related diseases

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Abstract

Background：Few previous studies have investigated the frequency of examinations for detecting cancer among outpatients with lifestyle-related diseases.
Methods：Outpatients with lifestyle-related diseases（hypertension, diabetes mellitus, dyslipidemia, and hyperuricemia）who were admitted to the metabolism and endocrinology, cardiovascular, or general medicine departments of Juntendo University Hospital from January 1, 2011 to December 31, 2013 were included in this study.
The frequency of examinations for detecting cancer was estimated for each 10-year age group, and the relation between various factors and the frequency of such examinations was then evaluated using the Cochran-Armitage trend test. Then, factors associated with the frequency of examinations for cancer were identified using multivariate logistic regression analysis.
Results：27,719 outpatients（mean age, 63 years；male sex, 60%）were surveyed based on their electronic medical records. Of these, 78% had diabetes, 64% had hypertension, 55% had dyslipidemia, and 17% had hyperuricemia. The following examinations were performed to detect cancer：lung cancer；chest X-rays 54% and computed tomography 11%：gastric cancer；contrast-enhanced upper gastrointestinal（GI）tract examinations 0.1% and upper GI endoscopy 4%：colorectal cancer；fecal occult blood tests 7% and colonoscopy 2%. Age and the number of lifestyle-related diseases were significantly associated with the frequency of examinations for cancer.
Conclusion：Our results indicated that the frequency of examinations for cancer was low in the clinical setting and that it was significantly associated with age and the number of lifestyle-related diseases. Although the Japanese health insurance system limits the screening of outpatients, more careful assessment of eligible patients might be required.
Keywords：Cancer, Secondary prevention, Preventive medicine, Epidemiology, Lifestyle-related disease

Introduction

The annual number of worldwide deaths from cancer has reached 8,200,000 people[1)]. In

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Japan, the number of cancer cases was reported to be 368,103 in 2014[2]. Thus, cancer is the most common cause of death in Japan at present, accounting for approximately 30% of all deaths[3].

Gastric cancer exhibits high mortality rates for both sexes in East Asia, Eastern Europe, and South America (particularly in Chile)[4]. Colorectal cancer is associated with high mortality rates for both sexes in North America, Australia, Europe, and Russia. In addition, lung cancer results in high male mortality rates in North America, Europe, and China and high female mortality rates in North America, Western Europe, China, and Oceania. In 2006, gastric, colorectal, and lung cancer were among the most common diseases affecting men ≥ 40 years of age in Japan. Similarly, gastric, colorectal, and lung cancer were among the most common diseases affecting women in their 50s[4]. Thus, these diseases place an important health burden on the middle-aged in Japan, and the importance of primary and secondary prevention, including health screening programs, for preventing cancer-related mortality has been emphasized.

However, examinations that aim to detect cancer are performed much less often in Japan than in Western countries[5)-7)]. In Europe and the United States, approximately 70% of adult women undergo breast and cervical cancer screening, whereas the equivalent figure for Japan is only about 30%[5)-7)]. Thus, low cancer examination rates have become a barrier to primary and secondary cancer prevention in Japan.

In such circumstances, it is important that the Japanese health insurance system allow early cancer detection among medical eligible outpatients who exhibit symptoms of cancer. In particular, patients with lifestyle-related diseases, such as diabetes or high blood pressure as well as middle-aged and elderly patients, should be targeted for such examinations[8]. In addition, regular outpatient visits would provide more opportunities to discover cancer. However, the Japanese health insurance system does not permit cancer screening examinations to be carried out for asymptomatic patients or those with no abnormal findings. Unfortunately, the early stages of some types of cancer are asymptomatic. Thus, in general medical clinics the early detection of cancer is considered to be difficult. On the other hand, patients who regularly attend medical institutions often undergo general medical examinations whenever necessary if they display any features associated with cancer.

As far as we know, no previous studies have investigated the frequency of cancer screening tests among outpatients with lifestyle-related diseases who visited Japanese medical institutions. The purpose of this study is to reveal the frequnecies of examinations aimed at detecting stomach, colon, or lung cancer and to identify the factors associated with the use of cancer screening tests among outpatients with lifestyle-related diseases.

Methods

Study population

This cross-sectional study screened outpatients who visited the Department of General Medicine, the Department of Metabolism and Endocrinology, or the Department of Internal Medicine of the Division of Cardiology at Juntendo University Hospital during the period from January 1, 2011 to December 31, 2013. Juntendo University Hospital is a general hospital in an urban district of Tokyo with over 1,000 beds that treats about 3,900 outpatients a day. Most of the outpatients who visit our

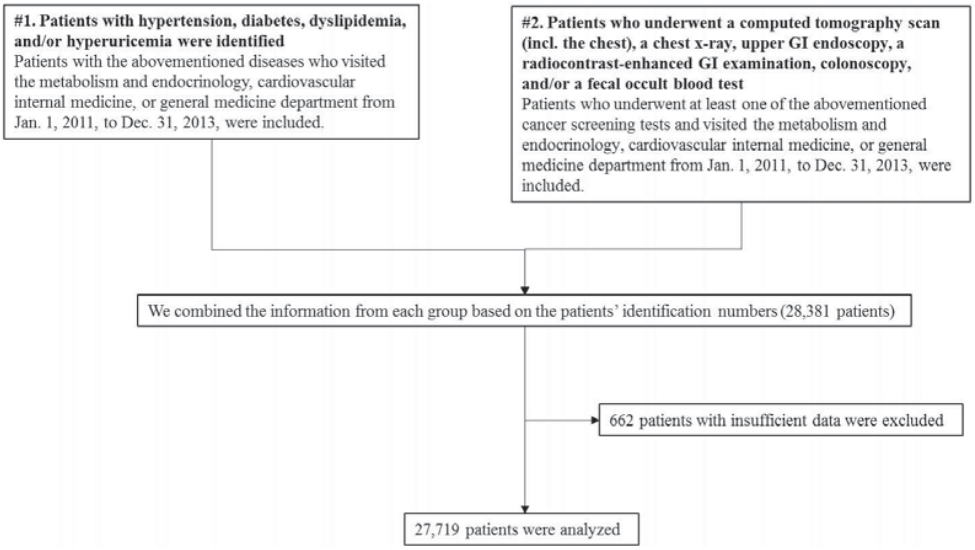

Figure 1 Flow of data collection and processing

institution are from the Tokyo metropolitan area or the Kanto region. Juntendo University Hospital adopted an electronic medical record system in January 2011. As a result, we are able to perform analyses of the data of tens of thousands of outpatients.

Data collection and processing

A flow diagram for this study is shown in Figure 1. From January 2011 to December 2013, the data of all patients who visited the Department of General Medicine, the Department of Metabolism and Endocrinology, or the Department of Internal Medicine of the Division of Cardiology at Juntendo University Hospital were investigated. First, hypertension, diabetes, dyslipidemia, and hyperuricemia/gout were defined as "lifestyle-related diseases". We then extracted the medical records of outpatients with lifestyle-related diseases from the hospital's electronic medical record database. In the present study, "examinations for cancer" were defined as examinations that were conducted when cancer was suspected or routine examinations that led to the discovery of cancer and were allowed by the Japanese medical insurance system. Next, we extracted the outpatients who had undergone screening tests for cancer. The "examinations for cancer" included chest x-rays or computed tomography (CT) scans that involved the chest for lung cancer, upper gastrointestinal (GI) endoscopy or radiocontrast-enhanced GI examinations for gastric cancer, and colonoscopy and fecal occult blood tests for colorectal cancer. The various types of information collected were then combined based on the patients' identification numbers, giving us 28,381 subjects. In total, 662 patients whose data were insufficient were excluded, leaving the data for 27,719 patients available for analysis. All of the examinations included in this study were performed because cancer was suspected or as a routine examination that led to the discovery of cancer, and none of them were aimed at specifically collecting data for the current study. The study protocol was approved by the institutional ethics committee (approval number : 2014108). This survey was conducted according to the ethics guidelines for epidemiological studies established by the Japanese government[9].

Table 1 Demographic characteristics

Characteristics	Mean ± Standard Deviation or n (%)
Number of participants	27719
Sex (male)	16650 (60)
Age (years)	63.1 ± 14.0
Lifestyle-related diseases	
Hypertension (%)	17613 (64)
Diabetes (%)	21522 (78)
Dyslipidemia (%)	15163 (55)
Hyperuricemia or gout (%)	4748 (17)
Cancer screening examinations	
Chest X-ray	14927 (54)
Computed tomography scan (incl. chest)	2976 (11)
Radiocontrast-enhanced GI examination	32 (0.1)
Upper GI endoscopy	1118 (4)
Fecal occult blood test	2078 (7)
Colonoscopy	661 (2)

Statistical analysis

The patients were stratified by age into 10-year age groups and according to the number of lifestyle-related diseases they had. The relation between these factors and the frequency of examinations for cancer were then evaluated using the Cochran-Armitage trend test. Factors that were significantly associated with the frequency of examinations for cancer were then determined using multivariate logistic regression analysis. The covariates examined in the multivariate analysis were age and the number of lifestyle-related diseases present. All calculations were performed using the JMP Pro software, version 11.0 (SAS Institute, Cary, NC, USA). Continuous data are reported as mean ± SD values. P-values of < 0.05 were considered to be statistically significant.

Results

Table 1 shows the demographic characteristics of the subjects of this cross-sectional study. A total of 27, 719 outpatients were analyzed (60% of the patients were male : mean age, 63.1 ± 14.0). The frequencies of each lifestyle-related disease were as follows : diabetes : 21,522 (78%), hypertension : 17,613 (64%), dyslipidemia : 15, 163 (55%), and hyperuricemia or gout : 4748 (17%). The number of patients that underwent tests for lung cancer is as follows : chest X-ray 14, 927 (54%) and computed tomography (including the chest) 2, 976 (11%). The number of patients that underwent tests for gastric cancer is as follows : upper GI endoscopy 1,118 (4%) and radiocontrast-enhanced GI examinations 32 (0.1%). The number of patients that underwent tests for colorectal cancer is as follows : fecal occult blood tests 2,078 (7%) and colonoscopy 661 (2%). The associations detected between the frequency of cancer examinations and age are shown in Table 2. As the patients' age increased, the frequencies of all of the examinations for detecting cancer, except radiocontrast-enhanced GI examination, rose. The associations detected between examinations for cancer and the number of lifestyle-related diseases are shown in Table 3. As the

Table 2 Percentage of participants that underwent examinations to review cancer stratified according to age groups

Age (years)	< 45	45-54	55-64	65-74	≥ 75	
	n (%) values					p-value*
Number of participants	3179	3672	6822	7948	6098	
Chest X-ray	1285 (40.4)	1737 (47.3)	3399 (49.8)	4539 (57.1)	3967 (65.1)	< 0.01
Computed tomography scan (incl. chest)	146 (4.6)	231 (6.3)	550 (8.1)	969 (12.2)	1080 (17.7)	< 0.01
Radiocontrast-enhanced GI examination	1 (0.03)	7 (0.19)	10 (0.15)	5 (0.06)	9 (0.15)	0.75
Upper GI endoscopy	48 (1.5)	106 (2.9)	254 (3.7)	423 (5.3)	287 (4.7)	< 0.01
Fecal occult blood test	160 (5.0)	216 (5.9)	455 (6.7)	629 (7.9)	618 (10.1)	< 0.01
Colonoscopy	26 (0.8)	44 (1.2)	145 (2.1)	242 (3.0)	154 (2.5)	< 0.01

* : according to the Cochran-Armitage trend test

Table 3 Percentages of participants that underwent examinations to review cancer stratified according to the number of lifestyle-related diseases

Number of lifestyle-related diseases	1	2	3	4	p-value*
Number of participants	9639	7280	8353	2447	
Chest X-ray	3799 (39.4)	4010 (55.1)	5461 (65.4)	1657 (67.7)	< 0.01
Computed tomography scan (incl. chest)	639 (6.6)	737 (10.1)	1141 (13.7)	459 (18.8)	< 0.01
Radiocontrast-enhanced GI examination	5 (0.05)	8 (0.11)	12 (0.14)	7 (0.29)	< 0.01
Upper GI endoscopy	282 (2.9)	323 (4.4)	357 (4.3)	156 (6.4)	< 0.01
Fecal occult blood test	473 (4.9)	549 (7.5)	728 (8.7)	328 (13.4)	< 0.01
Colonoscopy	156 (1.6)	169(2.3)	198 (2.4)	88 (3.6)	< 0.01

* : according to the Cochran-Armitage trend test

number of lifestyle-related diseases increased, the frequencies of examinations for cancer rose. The factors that were significantly associated with the frequency of examinations for cancer are listed in Table 4. Age was significantly associated with all types of examinations, except for radiocontrast-enhanced GI examinations. In the upper GI endoscopy and colonoscopy model, the odds ratios (OR) for the ≥ 45 age group were higher than those for the < 45 age group.

Regarding the number of lifestyle-related diseases, the frequencies of cancer examinations increased significantly as the number of lifestyle-related diseases rose in all models except the radiocontrast-enhanced GI examination model.

As for the number of cases of cancer detected among the study population, we first surveyed the patients that were diagnosed with or were suspected to have cancer based on their electronic medical records. As a result, we identified 449 patients (lung cancer 74, stomach cancer 251, and colon cancer 124). Then, we randomly selected 30 samples (lung cancer 10, stomach cancer 10, and colon cancer 10) and directly confirmed the diagnosis of cancer in these cases using each patient's medical record. Consequently, it was found that 10 patients had a history of cancer (lung cancer 6, stomach cancer 2, and colon cancer 2), and so we estimated that there were 119 patients who had a history of cancer among the study population (lung cancer 44, stomach cancer 50, and colon cancer 25) (0.43%).

Table 4-1 Factors associated with examinations to review cancer（binary logistic regression analysis）

	Chest X-rays		Computed Tomography Scans		Gastrointestinal Examinations	
Variables	OR（95%CI）		OR（95%CI）		OR（95%CI）	
Age（years）						
< 45	Reference		Reference		Reference	
45-54	1.15	（1.04-1.27）	1.25	（1.01-1.55）	5.05	（0.89-94.74）
55-64	1.18	（1.08-1.28）	1.53	（1.27-1.86）	3.47	（0.65-64.10）
65-74	1.51	（1.39-1.65）	2.35	（1.97-2.83）	1.40	（0.22-27.09）
≥ 75	2.05	（1.87-2.25）	3.56	（2.98-4.28）	3.17	（0.58-59.04）
Number of lifestyle-related diseases						
1	Reference		Reference		Reference	
2	1.80	（1.70-1.92）	1.45	（1.30-1.63）	2.06	（0.69-6.85）
3	2.65	（2.49-2.82）	1.87	（1.69-2.07）	2.70	（0.99-8.58）
4	2.90	（2.64-3.20）	2.69	（2.36-3.07）	5.51	（1.73-18.91）

OR；Odds ratio, 95%CI；95% confidence interval,

Table 4-2 Factors associated with examinations to review cancer（binary logistic regression analysis）

	Upper gastrointestinal Endoscopy		Fecal Occult Blood Tests		Fecal Occult Blood Tests	
Variables	OR（95%CI）		OR（95%CI）		OR（95%CI）	
Age（years）						
< 45	Reference		Reference		Reference	
45-54	1.83	（1.30-2.61）	1.07	（0.86-1.32）	1.39	（0.86-2.30）
55-64	2.30	（1.70-3.18）	1.15	（0.95-1.39）	2.41	（1.61-3.76）
65-74	3.29	（2.45-4.51）	1.33	（1.11-1.60）	3.42	（2.32-5.28）
≥ 75	2.86	（2.11-3.96）	1.71	（1.43-2.06）	2.80	（1.87-4.36）
Number of lifestyle-related diseases						
1	Reference		Reference		Reference	
2	1.42	（1.20-1.67）	1.52	（1.34-1.73）	1.32	（1.06-1.65）
3	1.29	（1.10-1.51）	1.71	（1.51-1.93）	1.27	（1.03-1.58）
4	1.92	（1.56-2.35）	2.75	（2.36-3.20）	1.89	（1.44-2.47）

OR；Odds ratio, 95%CI；95% confidence interval,

Discussion

This study detected low rates of examinations for cancer among outpatients with lifestyle-related diseases who regularly visited our hospital, and age and the number of lifestyle-related diseases were found to be significantly associated with the frequency of examinations for cancer. This is the first study to estimate the frequencies of examinations for cancer and to the reveal the factors associated with the frequency of such examinations among Japanese outpatients with lifestyle-related diseases.

Early detection and treatment are essential for combating cancer, which exhibits the highest mortality rate of all diseases in Japan. In fact, several previous studies have indicated that gastric screening might contribute to reducing the mortality rate of gastric cancer in Japan[10)-12)]. Despite this, cancer screening rates are low in Japan[7)]. Moreover, no studies have examined the frequency of cancer screening tests at general outpatient clinics[10)-12)].

During a literature search, we found few studies that had investigated the frequencies of examinations for cancer at outpatient clinics in Japan. One possible explanation for this lack of research is that the Japanese health insurance system does not allow cancer screening tests to be conducted for symptomless patients, which is a major barrier to screening in the clinical setting. Instead, specific health checkups are provided by the Japanese Government.

However, the Japan Public Health Center-based Prospective Study reported a 27% increase in the risk of cancer among men with a history of diabetes mellitus (hazard ratio [HR], 1.27 ; 95% confidence interval [CI], 1.14-1.42), and a borderline significant increase in the risk of cancer was noted for women (HR, 1.21 ; 95% CI, 0.99-1.47)[4]. A cohort study, which examined 99,565 Korean individuals who participated in a health examination program, reported that a particular metabolic risk profile (high serum glucose and total cholesterol levels and high blood pressure) was significantly associated with the colon cancer of men (HR, 1.40 ; 95% CI, 1.14-1.71)[13]. Therefore, outpatients with lifestyle-related diseases might be at high risk of several types of cancer, and it might be necessary to screen for these cancers to prevent cancer-related mortality. We estimated that there were 119 outpatients in the current study population with a history of cancer (0.43%). Thus, our results indicate the importance of screening for cancer among eligible outpatients in order to promote secondary cancer prevention in medical practice.

Our results showed that the number of lifestyle-related diseases and age were independent predictors of the frequency of examinations for cancer. It is widely known that having a combination of lifestyle-related diseases is a risk factor for heart disease, and greater attention should be paid to such patients[14)-16)]. Older adults are also generally considered to be at greater risk of illness[17]. Age-stratified cancer morbidity rate data collected in 2015 revealed that 60-year-old men are at a 16% risk of developing cancer by age 70 and that 70-year-old men are at a 30% risk of developing cancer by age 80. In comparison, 60-year-old women were found to be at a 9% risk of developing cancer by age 70, and 70-year-old women were shown to be at a 13% risk of developing cancer by age 80[18]. Both outpatients and physicians should become more aware of the need to perform examinations for cancer due to the effects of aging and lifestyle-related diseases. A post-hoc cross-sectional analysis reported that physicians who were treating patients with critical conditions paid more attention to their patients than physicians who were treating patients with less severe conditions[19]. Therefore, we also have to encourage primary and secondary cancer prevention among such outpatients.

Limitations

This study has some serious limitations. First, the Japanese health insurance system does not allow the use of examinations for detecting cancer among symptomless patients, which might have affected our results. In addition, we could not assess the frequency of voluntary health checkups. Further research that takes voluntary health checkups into account might be required. Another of the limitations relates to the diagnosis of patients with lifestyle-related diseases. In the current study, we defined patients who had been confirmed to have hypertension, hyperlipidemia, diabetes, hyperuricemia, or gout according to their electronic medical records as having lifestyle-related diseases. Because these patients were not diagnosed using the diagnostic criteria for each disease, we cannot determine whether they actually had the aforementioned diseases. Future study with adequate inclusion criteria involving a definitive diagnosis of lifestyle-related diseases is needed. The third limitation is that we did not investigate the reasons the tests were performed. We defined chest x-rays and CT scans as examinations that are used to detect lung cancer. As is well

known, x-rays and CT scans are also performed in cases in which lung cancer is not suspected；however, we did not consider whether the tests were conducted with the intention of searching for cancer. Future surveys of physicians are required to determine the reasons such examinations are performed. The fourth limitation is that we did not consider the patients' tumor status or the actual frequency of cancer screening examinations, although we estimated the numbers of outpatients with each type of cancer. Patients who were already visiting the hospital for cancer treatment or who underwent yearly examinations to screen for cancer are not likely to undergo additional tests to detect cancer. If such patients had accounted for a large proportion of the study sample, our results might have been affected by bias. A survey of outpatients is required to check the cancer treatment status of such patients and/or the frequency of yearly tests for cancer. Lastly, we could not collect data about various important factors, such as the subspecialty of each treating medical practitioner, whether the treating medical practitioner was a primary care provider, whether the patient was employed, etc. In future analysis, it will be necessary to include these items.

Conclusion

In a large-scale study involving about 30,000 patients, we determined that the frequency of examinations for cancer among outpatients with lifestyle-related diseases who visited our hospital was low. In addition, age and the number of lifestyle-related diseases were found to be significantly associated with the frequency of examinations for cancer. Although the Japanese health insurance system places limitations on the screening of outpatients, our results suggest the need for more careful assessment of eligible patients who exhibit symptoms of cancer and/or abnormal test results and more active encouragement of cancer screening among such outpatients.

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Conflict of interest The authors declare that they have no conflicts of interest.