

# 学位論文の要旨

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学位論文名 How Asymptomatic are Early Cancer Patients of Five Organs Based on Registry Data in Japan

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## 論文内容の要旨

### INTRODUCTION

The cancer screening rate is extremely low in Japan. Many Japanese people were diagnosed with cancer after visiting a medical institution because they presented with subjective symptoms. However, little is known about the relationship between symptoms and the cancer stage for several organs.

The aim of this study was to analyze symptom severity according to the cancer stage for five organs (stomach, colo-rectal, lung, breast and cervix). In addition, this study investigated the relationship between subjective symptoms and early detection.

### MATERIALS AND METHODS

#### *Cancer registry data*

Shimane Prefecture has been collecting hospital-based cancer registry data at Shimane University to improve cancer care. The authors used hospital-based cancer registry data collected between 2007 and 2013 by 13 hospitals.

In the hospital-based cancer registry, information on all primary cancer patients diagnosed or treated at the hospitals is collected by cancer registrars. Each registry item used in this study was based on the medical records according to the standard registry definition. The authors used the registration items, the site and histology code of the ICD-O-3, the stages of the UICC TNM system, route to discovery, and subjective symptoms at diagnosis.

Subjective symptoms were registered in cases of direct symptoms due to the tumor from the description of the medical record. Early stage cancer was defined as stages 0 and I in this study.

Of the 41,202 cases registered between 2007 and 2013, 35,076 initial-treatment cases were included in this study to avoid duplication among patients who visited multiple medical institutions. Overall, 30,985 data points were used for the analysis, and items that indicated final stages and unknown symptoms were excluded. Finally, a total of 18,405 data points were selected: 4,897 for stomach cancers, 6,614 for colorectal cancers, 3,481 for lung cancers, 2,514 for breast cancers, and 899 for cervical cancers.

### ***Statistical analysis***

The study protocol was approved by the Research Ethics Committee of Shimane University. And the authors obtained permission to use data from the Shimane Prefecture cancer registration review committee.

The percentages of symptomatic cases were compared using the chi-square test and Fisher's exact test. P-values < 0.05 were considered significant. A logistic regression model was used to calculate the odds ratio with a 95% confidence interval. The statistical analyses were conducted using JMP® 12 (SAS Institute Inc., Cary, NC, USA).

## **RESULTS AND DISCUSSION**

### ***Distribution of UICC TNM stages at diagnosis***

To evaluate early detection by organ, the distribution of the UICC TNM stages at diagnosis for both the Shimane data and the nationwide collection was examined. The percentage of early detection was defined as the number of cases diagnosed at stages 0 and I among all cases in this study.

The Shimane and the nationwide collections had similar stage distributions. Cervical cancer tended to be detected early, whereas the early detection of lung cancer was the least frequent among the five organs. However, the relative frequency of detection of stage IV lung cancer was 32.0%, which was higher than that of stage IV cancer in any of the other organs.

### ***The frequency of symptoms at each UICC TNM stage***

The proportion of symptomatic cases tended to increase as the cancer stage progressed in the five organs. The frequencies of symptomatic cases for each cancer stage showed different trends depending on the organ. For the stomach and colorectum, the frequencies of symptomatic cases at stages 0 and I were less than 50%, whereas the proportion at stage II was greater than 50%. Lung cancer had a lower proportion of symptomatic cases than cancer of any other organ at any stage from stages 0 to IV. The percentage of symptomatic cases for the lungs in stage IV was 81.9%, and approximately 20% of patients did not present subjective symptoms at the time of diagnosis. Breast tissue had the most subjective symptoms, and the symptomatic cases represented 44.7% even at stage 0. Cervical cancer has a symptomatic frequency exceeding 70% at the stage IB or higher, but a symptomatic frequency of only 20% to 30% in CIN3 to the stage IA.

### ***The relative frequencies of symptomatic cases in early cancer stages***

The frequencies of symptomatic cases in early cancer stages were low in the five organs. The frequency of symptomatic cases at an early cancer stage was the highest for breast at 30.2% and the lowest for lung at 8.2%. Compared with stomach cancer, the odds ratio of the subjective symptoms at the early cancer stage for breast cancer was the highest, at 1.26, and that for lung cancer was the lowest, at 0.26.

### ***Early detection in the symptomatic and asymptomatic groups***

The early detection rates for the symptomatic and asymptomatic groups were calculated. The early detection rates for the asymptomatic groups were higher than for the symptomatic groups for each organ. The percentage of early detection of stomach cancer among the asymptomatic group was 86.2%, whereas the percentage for the symptomatic group was 44.9%. Similar percentage of 74.9% and 34.2% were observed for colorectal cancer, 64.5% and 15.8% for lung cancer, 76.7% and 43.3% for breast cancer, and 98.8% and 55.9% for cervical cancer.

According to our survey, asymptomatic patients tended to be diagnosed earlier stage than symptomatic patients. Therefore, it is important for Japanese people to be screened for cancer even when they are asymptomatic.

Various cancer policies are proposed to reduce cancer mortality. Primary prevention reduces the cancer incidence by improving lifestyle habits and secondary prevention consists of cancer screening for early detection and early treatment. Early detection and early treatment can enhance the quality of life for patients through minimally invasive treatment. The evidence gained using cancer registration data is indispensable for effective cancer policies.

### **CONCLUSION**

To reduce the mortality rates, cancer must be detected and treated at an early stage. The results of this study show that the frequency of symptomatic cases tended to increase as the cancer stage progressed, and the frequency of symptomatic cases at the early stages of cancer were lower than those at advanced stages in the five organs. Therefore, the cancer may have already progressed when the patients received a consultation at a medical institution after the appearance of subjective symptoms.

Lung cancer was the least symptomatic and the most advanced at diagnosis among the five organs. Breast cancer was the most frequently symptomatic at the early stages, but the frequency was only 30%.

If patients are diagnosed asymptotically, the probability of the cancer being at an early stage is 77.6%, but if patients are diagnosed after symptoms appear, the probability of the cancer being at an early stage will drop to 36.1%. Thus, policy makers should inform people of the necessity of receiving cancer screening before they have symptoms.