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要旨

日本がん検診・診断学会誌16(3): 14-18、2009

本論で使う「がん検診」とは、市町村のがん対策として地域住民に対して実施される「対策型検診」と定義する。がん検診について、有名な8つの実施条件がある。そのうちの少なくとも2つの条件は登録精度の高い地域がん登録があってはじめて、効率的、継続的に把握できる。一つは罹患率である。がん検診は、罹患率・有病率・死亡率の高いがんに対して行われなければならない。当該地域住民を分母とするがん罹患率は、地域がん登録なくして知ることはできない。2つめは、感度・特異度・陽性反応適中度に代表される検査の精度指標である。がん検診は、高いレベルでバランスのとれた精度を持つ検査法で行われなければならない。感度・特異度を推計するためには、検診の見逃し例(偽陰性例)を知る必要がある。精度の高い地域がん登録があれば、検診受診者全員を直接追跡調査することなく、要精検者以外からのがんの発生を知ることができる。ほかに、がん検診の実施条件の一つである有効性は、がん死亡率の減少によって評価されるが、罹患率の推移が分からなければ、たとえば、がん死亡率の減少傾向を認めたとしても、それが早期発見の効果なのか、医療水準の向上のためか、罹患自体が減ったことによるのかを区別できない。

ところで、地域がん登録とは、特定の人口集団の一定期間における新規がん発生を把握し、罹患率を推計する仕組みのことである。がん罹患数は、国内比較、国際比較を容易にするため、がん罹患情報とがん死亡情報を用いて世界共通の方法で推計する。また、推計がん罹患数の確からしさを示す、DCO・DCN割合、I/M比などの世界共通の指標が存在する。日本の地域がん登録は、2008年6月現在、35道府県+広島市において地方公共団体事業として実施されているが、登録精度が世界標準に達しているのは長崎県と広島市だけであり、日本全体のがん罹患推計に用いられる登録も10地域前後にすぎない。

キーワード: がん、検診、罹患率

地域がん登録を用いた県内がん患者の医療機関受診に関する動態調査 ―診断時住所の医療圏と主治療医療機関の所在医療圏の関係について

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1．はじめに

がん医療においては、治療医療機関を集約化し、その治療内容と成績の均てん化が求められている。一方、地方では、治療内容や治療成績に関わらず居住地に近い医療機関を受診する傾向があり、治療医療機関の集約化は容易ではないと考えられている。

山形県は、村山、最上、置賜、庄内の4医療圏に区分されており、それぞれの医療圏がカバーする人口は、各々約57万人、9万人、24万人、31万人である。平成19年現在、がん診療連携拠点病院は、村山医療圏に3カ所、その他の医療圏に1カ所ずつ指定されている。庄内医療圏には既指定のがん診療連携拠点病院に相当する病院が他に1カ所あり、最上・置賜医療圏には既指定の病院以外、拠点病院の候補はない。

本報告では、診断時住所（居住地）の医療圏と主治療医療機関の所在医療圏との関係を、患者特性別に明らかにすることを目的とした。

2．対象と方法

集計対象は、2001－2003年に診断された登録患者21,450例のうち、上皮内がんおよび大腸mがん（869例）、DCN例（4,200例）、再発時のみの登録（272例）、疑診登録（7例）を除外した16,102例（75.1%）。主治療医療機関は、地域がん登録標準データベースシステムでは治療医療機関決定のルールに従って半自動的に決定される。主治療医療機関不明例は集計対象の10.3%であった。以上の集計対象を用いて、1. 居住地の医療圏が主治療医療機関の所在医療圏と同じかどうか、以下同様に、2. 性別、3. 年齢階級別（0-19、20-64、65-74、75-79、80-）、4. 進行度別（限局、領域、遠隔転移）、5. 部位別（胃・大腸・肝臓・乳房・肺とその他の部位6区分別）6. 発見経緯別（がん検診・人間ドック、通院中、その他・自覚症状）7. 治療法別（手術、化学療法、放射線治療）で特徴があるかを検討した。

3．結果

居住地の医療圏と主治療医療機関の所在医療圏が一致する割合で評価した。全体として、居住地が村山と庄内医療圏の例ではほぼ100%近く一致しており、最上医療圏で最も一致割合が低かった（71.1%）（図左上）。性別による違いは明らかでなかった（図左上）。年齢階級別では、最上や置賜医療圏のような一致割合の低い医療圏では、年齢が若いほど居住地と異なる医療圏で治療を受けている割合が高かった（図右上）。進展度別では、明らかな違いを認めなかったが、置賜医療圏では遠隔転移例ほど居住地と同じ医療圏で治療を受けている割合が高かった。部位別では、村山と庄内医療圏では部位による居住地と治療医療機関の医療圏に明らかな違いを認めなかったが、最

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上と置賜医療圏では違いがあった(図左下)。特に、肝臓やその他の部位のような罹患数の少ないがんにおいて居住地と治療医療機関の所在医療圏が異なる割合が高かった。発見経緯別では、明らかな違いを認めなかったが、最上医療圏では通院中例ほど居住地と同じ医療圏で治療を受けている割合が高かった。治療法別では、村山と庄内医療圏では治療法による居住地と治療医療機関の医療圏に明らかな違いを認めなかったが、最上と置賜医療圏では違いがあった。(図右下)。特に放射線治療を受けた症例で、居住地と治療医療機関の所在医療圏が異なる割合が高かった。

4．考察

本集計結果から、小さい医療圏に居住する人ほど、居住地域以外の医療圏で治療を受ける割合が高いことが分かった。この理由として、居住地の医療圏のがん医療機関数が足りない、がん治療内容が充足していない、などが考えられる。年齢が若い人、罹患数の少ない部位のがん、および各医療圏に放射線治療器があるにも関わらず放射線治療例において居住地と異なる医療圏の医療機関で治療を受ける割合が高かったことは、居住地に拠点病院相当の医療機関が1カ所しかなく、様々な要因でそこの医療では不足と思われる場合は、医療圏を越えて患者が移動することがあり得ることを示している。一方、本集計結果から、居住地に拠点病院相当の医療機関が複数存在することが、拠点病院に関わらず居住地域と同じ医療圏の医療機関を受診する行動と結びついている可能性も示唆された。

5．結語

地域がん登録資料を用いて、がん患者の居住地の医療圏と主治療医療機関の所在医療圏との関係について検討した。今後、このような受療動向と、2次医療圏に概ね1カ所に指定されているがん診療連携拠点病院の機能強化や機能分化の必要性を関連づけて考える必要があるだろう。

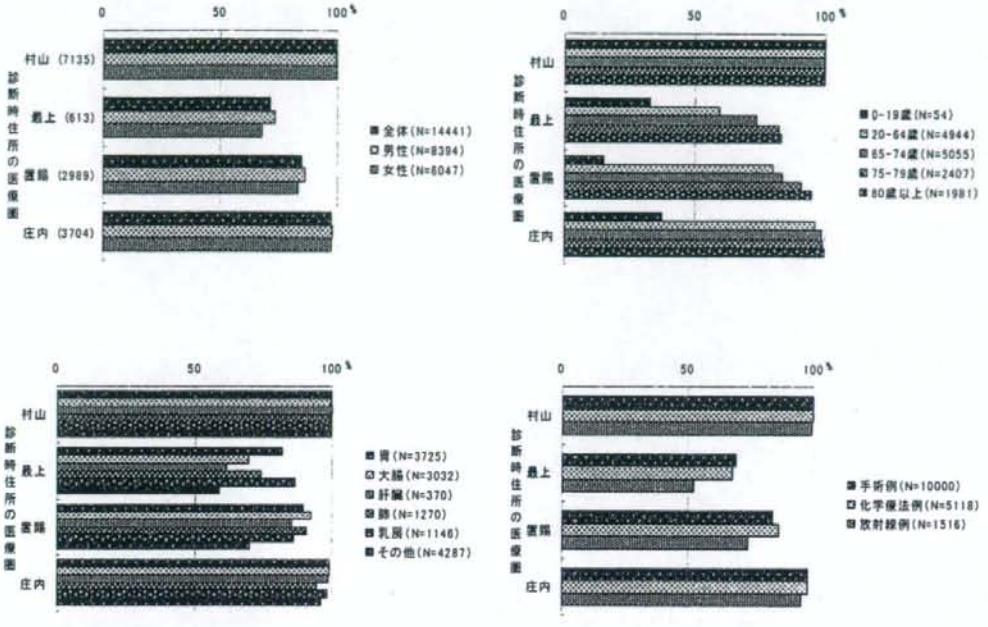

図　診断時住所の医療圏と主治療医療機関の所在医療圏が同じ割合
（左上：性別、右上：年齢階級別、左下：部位別、右下：治療法別）

Age-specific interval breast cancers in Japan: estimation of the proper sensitivity of screening using a population-based cancer registry

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The age-specific sensitivity of a screening program was investigated using a population-based cancer registry as a source of false-negative cancer cases. A population-based screening program for breast cancer was run using either clinical breast examinations (CBE) alone or mammography combined with CBE in the Miyagi Prefecture from 1997 to 2002. Interval cancers were newly identified by linking the screening records to the population-based cancer registry to estimate the number of false-negative cases of screening program. Among 112 071 women screened by mammography combined with CBE, the number of detected cancers, false-negative cases and the sensitivity were 289, 22 and 92.9%, respectively, based on the reports from participating municipalities. The number of newly found false-negative cases and corrected sensitivity when using the registry were 34 and 83.8%, respectively. In detected cancers, the sensitivity of screening by mammography combined with CBE in women ranging from 40 to 49 years of age based on a population-based cancer registry was much lower than that in women 50–59 and 60–69 years of age (40–49: 18, 71.4%, 50–59: 19, 85.8%, 60–69: 19, 87.2%). These data suggest that the accurate outcome of an evaluation of breast cancer screening must include the use of a population-based cancer registry for detecting false-negative cases. Screening by mammography combined with CBE may therefore not be sufficiently sensitive for women ranging from 40 to 49 years of age. (*Cancer Sci* 2008; 99: 2264–2267)

Breast cancer is the most common cancer among women in Japan.[1] A great deal of effort has been made to improve surgical and radiotherapeutic techniques as well as chemo-endocrine therapies for the management of breast cancer, although the mortality rate from breast cancer still remains high. The early detection of breast cancer is believed to be the best means of reducing this mortality and mammography is the only evidence-based screening technology currently available for this purpose. To reduce the mortality of breast cancer, Japan's Ministry of Health, Labor and Welfare declared in 2004 that mammography should be introduced for breast cancer screening in women 40 years of age or older. In addition, Japan's *National Cancer Act*, namely the law to promote cancer prevention and improve the quality of cancer screening, was also enforced in April 2007. Therefore, assessment of not only the screening modality, but also the accuracy of such screening programs has become increasingly important.

Although mammography is useful for detecting breast cancer in early stages, it is thought that the effectiveness of mammography screening in women from 40 to 49 years of age is lower than that in women 50 years of age and over.[2,3] The dense parenchyma in women before menopause can obscure tumor shadows and this results in the lower sensitivity of mammography screening in women 40–49 years of age.[4]

To calculate the proper sensitivity of the screening program, it is necessary to get hold of false-negative cases. A reporting system for false-negative cases from participating municipalities was established in Miyagi Prefecture. However, the report was not a legal duty for the municipalities, so the true number of false-negative cases was difficult to determine.

Interval cancers are cases that are diagnosed with no evidence of cancer in the primary screening, but they are diagnosed as breast cancer until further screening can be conducted. Generally speaking, interval cancer does not always indicate a false-negative case. However, determining the precise number of cases of interval cancer is worthwhile for estimating the proper sensitivity of mammography screening.[5] The present study compared the list of all women screened at Miyagi Cancer Screening Center with a population-based cancer registry covering the study areas to determine the precise number of cases of interval cancer. These data were used to calculate the proper sensitivity of breast cancer screening based on the age of the patient and screening method.

The purpose of the present study is to estimate age-specific sensitivity using a population-based cancer registry in Japan. Organizing a cancer registry takes a lot of time and effort, but it is almost impossible to obtain accurate statistics regarding cancer screening without using a cancer registry. When Japan's *National Cancer Act* came into force in April 2007, assessment of the screening task became of primary importance. However, there have been no reports evaluating the precise sensitivity of breast cancer screening using the cancer registry. With the use of a population-based cancer registry in Miyagi Prefecture, we investigated age-specific interval cancers to estimate precise sensitivity of mammography screening conducted in women aged not only 50–69 years, but also 40–49 years. The present study indicates that mammography screening may not be sufficiently sensitive for women aged 40–49 years. This study will help us to establish an optimal breast cancer screening system on the basis of proper sensitivity of mammographic screening in Japan.

Subjects and Methods

Study subjects. Biennial clinical breast examinations (CBE) alone or CBE combined with mammography were performed

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for all participants requesting screening in Miyagi Prefecture[6] from January 1997 to December 2002. There were 112 071 eligible women in the mammography combined with CBE group (20 587 women aged 40–49, 47 728 women aged 50–59 and 43 756 women aged 60–69) and 236 839 women in the CBE alone group (103 926 women aged 40–49, 65 529 women aged 50–59 and 67 384 women aged 60–69). On the basis of screening history, 13% of the participants were 'initial', or without screening history, and 87% were 'subsequent', or were previous participants in the screening program.

Screening methods. The screening system included mediolateral oblique imaging of both breasts performed in mobile vans equipped with the mammography system. CBE were conducted simultaneously with interpretation of the mammograms. The mammograms were subsequently re-evaluated by two authorized screeners at Miyagi Cancer Screening Center. The findings of the CBE and mammograms were classified into five categories: Category 1, negative; Category 2, benign finding(s); Category 3, probably benign finding(s); Category 4, suspicious abnormality; Category 5, malignancy. The women who were rated in Category 3 or higher by the CBE and/or mammography were referred for diagnostic examinations.

Breast density was later graded by a single examiner according to criteria for Breast Imaging Reporting and Data System (BI-RADS) mammography density categories:[7,8] < 25% dense for almost entirely fatty (Category 1), 25–50% dense for scattered fibroglandular densities that could obscure a lesion on a mammogram (Category 2), 51–75% for heterogeneously dense, which may lower the sensitivity of mammography (Category 3), and > 75% dense for the extremely dense breast, which lowers the sensitivity of mammography (Category 4).

Identification of cancer cases. All results of diagnostic examinations were reported by the hospitals that performed the diagnostic mammography and/or ultrasonography (biopsy and/or surgical operation if necessary). Screen-detected cancer was defined as a case diagnosed pathologically within 6 months after a positive screening test (detected cases). Interval cancers are defined as cases that were diagnosed as no malignancy in the primary screening, but were clinically diagnosed as breast cancer during the screening interval (2 years) until the subsequent screening was conducted. We regarded interval cancers as false-negative cases in this study. Therefore, the false-negative rate was defined as the proportion of interval cancers in 2 years after screening out of the sum of interval cancers and all screen-detected cancers. Information was obtained on false-negative cases using the reports from participating municipalities. When the reports were received, they were referred to the hospital to obtain information concerning the cases (reported cases).

Interval cancers were newly identified in this study by linking the screening records to the population-based cancer registry data for incident breast cancers in Miyagi Prefecture (registered cases). The death certificate only (DCO) rate is an important factor to confirm the reliability of the cancer registry. The DCO rate in Miyagi Prefecture is 2.7%, indicating that the data for registered cases are of relatively high reliability.[9] The matching of records from the screening database with the cancer registry was carried out with the aid of registry officials. Name, address and date of birth were used to identify individuals. This study was conducted in accordance with the principles specified in the Declaration of Helsinki. All procedures and analyses of the individual records were evaluated and approved by the ethical committee of Tohoku University.

Sensitivity of mammography and CBE. Screening sensitivity is defined as the number of screen-detected cancers expressed as a proportion of the total cancer incidence (screen detected plus interval cancers) in women screened. The sensitivity was calculated for all age groups (40–49, 50–59, and 60–69) for each method; i.e. mammography based screening and CBE alone.

Table 1. Recall rate, detected cancers and detection rates for the two screening and three age groups

	Subject	Recall rate	Detected cancers	Detection rate
MMG with CBE				
40–49	20 587	11.6%	45	0.22%
50–59	47 728	9.5%	115	0.24%
60–69	43 756	7.2%	129	0.29%
CBE alone				
40–49	103 926	8.1%	131	0.13%
50–59	65 529	4.9%	68	0.10%
60–69	67 384	3.6%	82	0.12%

MMG, mammography; CBE, clinical breast examination.

Results

Table 1 compares the recall rates for the diagnostic examinations and detection rates of breast cancer, according to the two screening groups and the three age groups. Among women aged 40–49 years screened by mammography combined with a CBE, the recall rate and detection rate were 11.6% and 0.22%, respectively. In women aged 50–59 years, the respective recall and detection rates were 9.5%, 0.24%. In women aged 60–69 years, the respective recall and detection rates were 7.2% and 0.29%. Over 99% of patients had visited hospitals for further examination in all age groups. The recall rate in screening generally declined with increasing age. Among women screened by CBE alone, the recall rate of women aged 40–49 years was significantly higher than that of women aged 50 and over, but detection rate of cancer was almost the same in the three groups.

Thirty-five interval cancer cases were newly identified in the mammography with CBE group, and 137 cases in the CBE alone group based on the population-based cancer registry. There were 2, 9 and 10 reported interval cancer cases for age 40–49, 50–59 and 60–69 groups, respectively, in the mammography with CBE group. The total number of interval cancers was therefore 18, 19 and 19, respectively, for each group. Similarly, 21, 11, 15, interval cancer cases were revised to 79, 47 and 58 in the CBE alone group for women aged 40–49, 50–59 and 60–69 groups, respectively (Table 2). The proportion of early breast cancer in the mammography with CBE group was 81.4% in the screening detected group and 58.5% in the interval cancer group. On the other hand, early breast cancer rate in the CBE alone group was 69.2% in the screening detected group, and 47.5% in the interval cancer group. Among the mammography combined with CBE group, the lowest sensitivity (71.4%) was observed in the 40–49 years group. The sensitivity in the 50–59 and 60–69 groups were 85.8% and 87.2%, respectively. According to the results of χ^2 test, the sensitivity in the 40–49 years group was statistically significantly lower than other older groups. In contrast, the sensitivity of CBE alone was almost the same value in the three age groups, and these values were much lower than that of the 40–49 years group with mammography. There was no statistical significance of age in CBE alone groups. On the other hand, mammography with CBE groups were significantly more sensitive than CBE alone groups in 50–59 and 60–69 years of age. However, there was no significant difference between the mammography with CBE group and CBE alone group for women 40–49 years of age.

Table 3 shows the sensitivity of mammography in association with different breast densities and ages. Among women 40–49 years of age, the sensitivities in extremely dense and dense breasts were 50.0% and 60.0%, respectively. In women 50–59 years of age, the sensitivities in extremely dense and dense breasts were 50.0% and 66.7%, respectively. In women 60–69 years of

Table 2. Sensitivity, specificity and positive predictive value according to the two screening groups and three age groups

Methods and age groups	MMG with CBE			CBE alone		
	40–49	50–59	60–69	40–49	50–59	60–69
Detected cancer	45	115	129	131	68	82
Reported interval cancers	2	9	10	21	11	15
Provisional sensitivity	95.7%	92.0%	92.8%	86.2%	86.1%	84.5%
Specificity	88.6%	90.7%	93.1%	92.0%	95.2%	96.5%
PPV	1.9	2.5	4.1	1.6	2.1	3.4
Interval cancers from population-based cancer registry	16	10	9	58	36	43
Total interval cancers	18	19	19	79	47	58
Proper sensitivity	71.4%	85.8%	87.2%	62.4%	59.1%	59.9%

CBE: clinical breast examination, MMG: mammography, PPV: positive predictive value.

Table 3. Sensitivity of mammography in association with different breast densities and ages

Age group (years)	Breast density (BI-RADS[‡] category)			
	1	2	3	4
40–49[†]	100.0% (1/1)	69.2% (9/13)	60.0% (15/25)	50.0% (10/20)
50–59	87.5% (7/8)	80.7% (46/57)	66.7% (34/51)	50.0% (9/18)
60–69	91.2% (31/34)	79.7% (63/79)	78.6% (22/28)	57.1% (4/7)
Total	90.7% (39/43)	79.2% (118/143)	68.3% (71/104)	51.1% (23/45)

[†]Four data are lacking because of missed mammography.
[‡]BI-RADS: Breast Imaging Reporting and Data System.

age, the sensitivities in extremely dense and dense breasts were 57.1% and 78.6%, respectively. Sensitivity according to BI-RADS category was statistically significant (p-value < 0.001, x^2 test).

Discussion

Breast screening has been an important means of decreasing breast cancer mortality and mammography is the only evidence-based screening technology currently available for this purpose. Several randomized trials of mammography screening showed that the usefulness of mammography screening in women aged 50 and over is statistically obvious; however, the effectiveness in women aged 40–49 is controversial.[2,3] The purpose of this study is to estimate age-specific sensitivity using a population-based cancer registry in Japan.

Reducing mortality from specific cancer is the most important index of the cancer screening, but it will take several decades to show the true effectiveness of screening. In the present study, we adopted interval cancers as an important indicator of the quality of a breast cancer screening program and as a predictor for its success in reducing breast cancer mortality.[5] In general, interval cancer does not always indicate a false-negative case. However, we regarded interval cancers as false-negative cases in this study because a population-based screening program should be responsible for a participant's health until further screening. The number of interval cancer cases from participating municipalities was very small. The provisional sensitivity of screening using mammography with CBE in woman 40–49 years of age is 95.8% based on the data from the participating municipalities. After using the cancer registry, the sensitivity went down to 71.4% in women 40–49 years of age. In the Age Trial[10] a randomized controlled trial that was designed specifically to study the benefit of starting mammography screening from age 40, the sensitivity of first screening was reported as 73.6%. Fracheboud *et al.*[11] reported observation of 1002 interval cancers within 2 years of screening whereas the number of screening-detected cancers was 3639 cases. This means that of all breast cancers diagnosed in regular participants, 64% will be detected by screening and 34% will emerge as interval cancers. Our results are in line with previous studies.

The sensitivity in the 40–49 years group was significantly lower than other older groups as shown in Table 2. Several factors were discussed as the reason for this. The first of those factors is the dense parenchyma in women before menopause. Breast masses are indicated by their density in the mammography, so that the masses are often hidden in a dense breast. A previous study by Kolb[12] showed a low sensitivity, 47.8% and 58.0%, in dense breast screening and in women under 50. These types of interval cancers are true false negatives. A great deal of effort has been made to decrease this type of interval cancer; digital mammography may be one of the useful candidates for overcoming this problem. Pisano *et al.*[13] showed that the overall diagnostic accuracy of digital and film mammography as a means of screening for breast cancer is similar, but digital mammography is more accurate in women under the age of 50 years, women with radiographically dense breasts and premenopausal or perimenopausal women. Further technological improvement is expected in this field.

The second factor is the unexpected, rapid, aggressive growth of tumors in younger women. Weedon-Fekjær *et al.*[14] reported a large variation in breast cancer tumor growth, with faster growth among younger women. This type of interval cancer may not be a false-negative case, but this type of cancer often results in a bad end. Further study on the suitable interval of screening program in younger women may be needed.

Although the sensitivity of screening using mammography with CBE in the 40–49 years of age group was lower than older groups, the sensitivity was relatively higher than screening with CBE alone in the 40–49 years of age group. Among the older groups, the sensitivities were statistically significantly higher in the mammography with CBE groups than CBE alone groups. The effectiveness of mammography is beyond doubt from the viewpoint of sensitivity in the 50–69 years of age group. On the other hand, we may need to consider introducing new modality

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to the screening program for younger women in order to find cancers at an earlier stage.

Ultrasonography is one of the candidates for this purpose because it is able to detect breast cancer at early stage based on the mass shape even in the dense parenchyma of women before menopause. In a study of 374 women using a state cancer registry, Moy *et al.*[15] reported only six (2.6%) women that had cancer that was not detected by either mammography or ultrasonography. The accuracy of ultrasonography tends to depend on the experience of the screener, so that it is important to provide training systems and diagnostic lexicons in breast cancer screening.

The American College of Radiology Imaging Network (ACRIN), a multicenter protocol to assess the efficacy of screening breast ultrasonography, began enrollment for high-risk asymptomatic women with dense breasts for three annual screening mammograms and ultrasonography independently in April, 2004, to determine the true measures of the performance of screening ultrasonography.[16] It is anticipated that mammography and ultrasonography will complement each other.

The Ministry of Health, Labor and Welfare of Japan launched a national priority research program, entitled 'Randomized controlled trial on effectiveness of ultrasonography for breast cancer screening' in 2007. To verify the quality and effectiveness of ultrasonograohy for breast cancer screening, 120 000 women aged 40–49 years will be enrolled, with randomization into two groups, mammography with ultrasonography and mammography alone. The first endpoints of this trial are sensitivity and specificity, and the secondary endpoint is the cumulative rate of advanced breast cancer in the two groups. Using a cancer registry is necessary to identify the false-negative cancer cases and accurately estimate the sensitivity of screening. This trial, designated the Japan Strategic Anticancer Randomized Trial (J-START), is the first large-scale RCT of cancer screening in Japan, following enforcement of the *National Cancer Act* in 2007.

In conclusion, mammography is considered to be an effective screening method in comparison with CBE, especially in the 50–69 years of age group. However, screening by mammography combined with CBE may not be sufficiently sensitive for women between 40 and 49 years of age. Adding other screening modalities should therefore be further discussed to establish an optimal sensitive screening protocol.

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Original Contribution

Coffee Consumption and the Risk of Oral, Pharyngeal, and Esophageal Cancers in Japan

The Miyagi Cohort Study

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An inverse association between coffee consumption and the risk of oral, pharyngeal, and esophageal cancers has been suggested in case-control studies, but few results from prospective studies are available. Data from the Miyagi Cohort Study in Japan were used to clarify the association between coffee consumption and the risk of these cancers. Information about coffee consumption was obtained from self-administered food frequency questionnaires in 1990. Among 38,679 subjects aged 40–64 years with no previous history of cancer, 157 cases of oral, pharyngeal, and esophageal cancers were identified during 13.6 years of follow-up. Hazard ratios were estimated by the Cox proportional hazards regression model. The risk of oral, pharyngeal, and esophageal cancers was inversely associated with coffee consumption. The multivariate-adjusted hazard ratio of these cancers for ≥1 cups of coffee per day compared with no consumption was 0.51 (95% confidence interval: 0.33, 0.77). This inverse association was consistent regardless of sex and cancer site and was observed both for subjects who did not drink or smoke and for those who currently drank or smoked at baseline. In conclusion, coffee consumption was associated with a lower risk of oral, pharyngeal, and esophageal cancers, even in the group at high risk of these cancers.

carcinoma, squamous cell; coffee; cohort studies; esophageal neoplasms; Japan; mouth neoplasms; pharyngeal neoplasms; risk

Abbreviation: CI, confidence interval.

Although both alcohol and tobacco are strongly established risk factors for oral, pharyngeal, and esophageal cancers, the factors protective against these cancers are not well known; high-level consumption of fresh vegetables and fruit may decrease the risk (1–3). Further evidence for the primary prevention of oral, pharyngeal, and esophageal cancers is needed, since quality of life for patients with these cancers is strongly affected (4), and fatality rates for esophageal cancer are relatively high (1–3).

Coffee is considered to help protect against cancer through the activity of its anticarcinogenic constituents (4–7). Numerous epidemiologic studies, mostly with a case-control design, have investigated the relation between coffee consumption and the risk of oral, pharyngeal, and esophageal cancers (8–21), but the results have been inconsistent. The latest 2 case-control studies in Italy and Switzerland suggested a significant inverse association between coffee consumption and the risk of cancers of the oral cavity, pharynx, and esophagus (18, 19). However, case-control studies are not free from selection bias or recall bias related to the retrospective assessment of coffee consumption and other lifestyle-related factors after a diagnosis of cancer. By contrast, results from prospective cohort studies have been few: one suggested no association (20), and another reported an inverse association for buccal cavity and pharyngeal cancers (21).

We therefore conducted a population-based, prospective cohort study in Japan, where consumption of coffee is

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relatively high (22) and the incidence of esophageal cancer in men is also high (1, 23). Our aim was to investigate the association between coffee consumption and the risk of oral, pharyngeal, and esophageal cancers.

MATERIALS AND METHODS

Study cohort

Our study was based on the Miyagi Cohort Study, the design of which has been described in detail elsewhere (24). Briefly, all 51,921 residents (25,279 men and 26,642 women) aged 40–64 years living in 14 municipalities randomly selected from the 62 in Miyagi Prefecture, northeastern Japan, were entered into the study as cohort subjects on April 1, 1990. From June through August 1990, we delivered self-administered questionnaires to them on various health habits. The questionnaires were delivered to, and collected from, the subjects' residences by members of health-promotion committees appointed by the municipal governments. Usable questionnaires were returned by 47,605 subjects (22,836 men and 24,769 women); the response rate was 91.7%. Because all residents in the study area had been entered as cohort subjects and the rate of response to the questionnaires was very high, we considered our subjects sufficiently representative of the area. The study protocol was approved by the institutional review board of Tohoku University School of Medicine. We considered the return of self-administered questionnaires signed by the subjects to imply their consent to participate in the study.

Dietary assessment

Dietary intake was assessed by a baseline survey that used a self-administered food frequency questionnaire. In this questionnaire, we asked participants to report their frequency of recent consumption of 36 food items and 4 beverages, including coffee. The questionnaire provided 5 categories of response to describe participants' frequency of coffee consumption: never, occasionally, 1 to 2 cups/day, 3 to 4 cups/day, and 5 or more cups/day. No questions were asked about the type of coffee used, the method of brewing, or the temperature of the beverage. The volume of a typical cup of coffee was 150 mL. The questionnaire also included details of personal and family history of disease, physical status, drinking and smoking habits, and occupational and educational status.

The reproducibility and validity of coffee consumption data among these subjects has been reported previously (25). Spearman's rank correlation coefficient for the correlation between consumption as assessed by the food frequency questionnaire and four 3-day diet records was 0.70, and that between consumption measured by 2 food frequency questionnaires during the 1-year interval was 0.72.

Recording of cancer cases, follow-up

The endpoint of our analysis was the incidence of either oral, pharyngeal, or esophageal cancer defined by topography codes—C00.0–09.9 (lip and oral cavity), C10.0–10.9 and C12.9–14.8 (pharynx), and C15.0–15.9 (esophagus)—in accordance with the *International Classification of Diseases for Oncology*, Second Edition. We excluded cancer of the nasopharynx (C11.0–11.9) from the pharyngeal cancer classification.

We ascertained the incidence of cancer through computerized record linkage to the Miyagi Prefecture Cancer Registry, one of the oldest and most accurate population-based cancer registries in Japan (26). Between 1993 and 1997, the percentage registered by death certificates only for oral cavity cancer was 7% for men and women; for esophageal cancer, these values were 10% for men and 20% for women (26).

Of the 47,605 subjects who responded to the questionnaire, we excluded 1,146 (441 men and 705 women) who had been given a diagnosis of cancer before the baseline survey was conducted, as ascertained from self-reports and the cancer registry. We also excluded 7,780 subjects (3,537 men and 4,243 women) who had entered incomplete responses about coffee consumption. Consequently, data for 38,679 eligible subjects (18,858 men and 19,821 women), including 157 subjects (135 men and 22 women) with oral, pharyngeal, or esophageal cancer, were entered into the analysis.

For follow-up, we established a follow-up committee that consisted of the Miyagi Cancer Society, the community health divisions of all 14 municipalities, the Department of Health and Welfare of Miyagi Prefectural Government, and the Division of Epidemiology, Tohoku University School of Medicine. The committee periodically reviewed the residential registration records of each municipality. From this review, we identified subjects who had either died or emigrated during the observation period. Follow-up of subjects who had moved from the study municipalities was discontinued because the committee could not review the residential registration records from outside the study area. During the study period, 2,207 subjects (1,051 men and 1,156 women: 5.7% of the total) were lost to follow-up.

Statistical analysis

We counted person-years of follow-up for each of the subjects from June 1, 1990, until the date of diagnosis of oral, pharyngeal, or esophageal cancer; the date of emigration from the study area; the date of death; or the end of the follow-up period (December 31, 2003), whichever occurred first. The mean follow-up period was 12.8 years, and the maximum follow-up period was 13.6 years.

We combined the upper 3 categories of coffee consumption (1 to 2 cups/day, 3 to 4 cups/day, and 5 or more cups/day) into the single category "1 or more cups/day" because of the small number of subjects and cases in each category. We chose the nonintake category (subjects who responded "never" to coffee consumption) as the reference group. We used the Cox proportional hazards regression model to estimate hazard ratios and 95% confidence intervals of oral, pharyngeal, and esophageal cancer incidence according to categories of coffee consumption and to adjust for potentially confounding variables; SAS version 9.1 statistical software (SAS Institute, Inc., Cary, North Carolina) was

used. The P values for the analysis of linear trends were calculated by treating the coffee consumption category as a continuous variable. All reported P values were 2-sided and were considered statistically significant if less than 0.05. All analyses were conducted for total subjects and separately by sex. We also performed separate analyses after dividing cases of cancer into oral and pharyngeal (*International Classification of Diseases for Oncology*, Second Edition codes C00.–09.9, C10.0–10.9, and C12.9–14.8) and esophageal (C15.0–15.9).

We considered the following variables to be potential confounders: age (in years), sex, body mass index (<18.5 kg/m^2, 18.5–24.9 kg/m^2, ≥25.0 kg/m^2), alcohol consumption (never, former drinker, current drinker consuming <45.6 g ethanol/day, current drinker consuming ≥45.6 g ethanol/day), cigarette smoking (never smoked, former smoker, current smoker of <20 cigarettes/day, current smoker of ≥20 cigarettes/day), consumption of vegetables and fruit (<2 times/month, 1–2 times/week, 3–4 times/week, every day), and green tea consumption (<1 cup/day, 1–2 cups/day, 3–4 cups/day, ≥5 cups/day).

We performed additional analyses after we had restricted cases of cancer to histologically confirmed squamous cell carcinoma (defined as morphology codes 8050/0 to 8082/3 according to the *International Classification of Diseases for Oncology*, Second Edition) of the oral cavity, pharynx, and esophagus and after exclusion of all subjects who had been given a diagnosis of oral, pharyngeal, or esophageal cancer within the first 3 years of follow-up. Analyses were stratified by alcohol consumption status and by cigarette smoking status at baseline.

RESULTS

During 494,935 person-years of follow-up (238,731 for men and 256,204 for women), we documented 157 cases of oral, pharyngeal, or esophageal cancer (135 men and 22 women). Included were 48 cases of oral or pharyngeal cancer (31 men and 17 women) and 112 cases of esophageal cancer (106 men and 6 women).

The characteristics of the subjects at baseline, as categorized by coffee consumption, are presented in Table 1. Subjects with higher coffee consumption tended to be younger and have a body mass index of 18.5–24.9 kg/m^2. Higher coffee consumption was associated with a higher frequency of smoking, lower vegetable consumption, and lower green tea consumption by both men and women. For women, higher coffee consumption was also associated with higher alcohol consumption (data not shown).

Table 2 presents the association between coffee consumption and the combined incidence risk of cancers of the oral cavity, pharynx, and esophagus. We found a significant inverse association between coffee consumption and the combined incidence risk of oral, pharyngeal, and esophageal cancers for both men and women. The multivariate-adjusted hazard ratios of oral, pharyngeal, and esophageal cancer incidence for 1 or more cups of coffee per day compared with no consumption were 0.51 (95% confidence interval (CI): 0.33, 0.77; P for trend = 0.002) for all subjects, 0.59 (95% CI: 0.38, 0.91; P for trend = 0.03) for men, and 0.17 (95% CI: 0.04, 0.69; P for trend = 0.01) for women.

There were 132 cases of squamous cell carcinoma of the oral cavity, pharynx, or esophagus; this condition therefore accounted for more than 80% of the cancers in the 3 areas. When we restricted our analysis to these 132 cases alone, the result did not differ from that for all cancer cases

Table 1. Characteristics of Study Subjects (N = 38,679) According to Coffee Consumption Status, Miyagi, Japan, 1990–2003

Characteristic	Coffee Consumption		
	Never	Occasionally	≥1 Cup/Day
No. of subjects	6,949	14,118	17,612
Mean age, years (SD)	54.2 (7.0)	52.8 (7.2)	48.9 (7.1)
Men, %	47.1	46.8	51.0
Body mass index, %			
<18.5 kg/m^2	2.7	2.0	2.4
18.5–24.9 kg/m^2	65.1	67.2	71.2
≥25.0 kg/m^2	32.3	30.8	26.4
Alcohol consumption, %			
Never	45.3	43.0	38.4
Former	6.5	5.0	5.3
Current (<45.6 g ethanol/day)	38.9	45.1	49.6
Current (≥45.6 g ethanol/day)	9.3	6.9	6.6
Cigarette smoking, %			
Never	55.9	54.6	46.1
Former	13.7	12.4	10.0
Current (<20 cigarettes/day)	12.2	12.7	12.8
Current (≥20 cigarettes/day)	18.3	20.4	31.1
Vegetable consumption,[a] %			
≤2 times/month	3.4	2.8	2.8
1–2 times/week	15.7	15.7	17.6
3–4 times/week	31.6	35.2	37.5
Every day	49.4	46.2	42.1
Fruit consumption,[b] %			
≤2 times/month	13.1	8.9	8.8
1–2 times/week	19.7	19.8	20.1
3–4 times/week	24.7	29.0	29.5
Every day	42.6	42.2	41.5
Green tea consumption, %			
<1 cup/day	32.6	27.0	32.2
1–2 cups/day	19.4	20.8	28.2
3–4 cups/day	20.0	23.2	20.8
≥5 cups/day	27.9	29.0	18.9

Abbreviation: SD, standard deviation.

[a] The maximum intake of spinach, carrot or pumpkin, tomato, and cabbage and Chinese cabbage.

[b] The maximum intake of oranges, other fruits, and fruit juice.

Table 2. Hazard Ratios and 95% Confidence Intervals of the Incidence of Cancer of the Oral Cavity, Pharynx and Esophagus Combined According to Coffee Consumption, Miyagi, Japan, 1990–2003

	Coffee Consumption			*P* for Trend[a]
	Never	Occasionally	≥1 Cup/Day	
All subjects				
No. of person-years	88,205	181,569	225,160	
No. of incident cases	53	53	51	
Multivariate-adjusted hazard ratio[b]	1.00	0.54	0.51	0.002
95% confidence interval	Reference	0.37, 0.80	0.33, 0.77	
Sex				
Men				
No. of person-years	40,958	83,963	113,809	
No. of incident cases	44	43	48	
Multivariate-adjusted hazard ratio[b]	1.00	0.54	0.59	0.03
95% confidence interval	Reference	0.35, 0.82	0.38, 0.91	
Women				
No. of person-years	47,247	97,607	111,350	
No. of incident cases	9	10	3	
Multivariate-adjusted hazard ratio[b]	1.00	0.58	0.17	0.01
95% confidence interval	Reference	0.23, 1.49	0.04, 0.69	
Squamous cell carcinoma[c]				
No. of person-years	88,234	181,598	225,173	
No. of incident cases	44	43	45	
Multivariate-adjusted hazard ratio[b]	1.00	0.51	0.51	0.005
95% confidence interval	Reference	0.33, 0.78	0.33, 0.80	

[a] *P* values were calculated by treating the coffee consumption category as a continuous variable and as 2-sided.

[b] Adjusted for age (in years), sex, body mass index (<18.5, 18.5–24.9, ≥25.0 kg/m^2), alcohol consumption (never, former drinker, current drinker of <45.6 g ethanol/day, current drinker of ≥45.6 g ethanol/day), cigarette smoking (never smoked, former smoker, current smoker of <20 cigarettes/day, current smoker of ≥20 cigarettes/day), consumption of vegetables and fruits (≤2 times/month, 1–2 times/week, 3–4 times/week, every day), and green tea consumption (<1 cup/day, 1–2 cups/day, 3–4 cups/day, ≥5 cups/day).

[c] Cancer cases restricted to histologically confirmed squamous cell carcinoma of the oral cavity, pharynx, and esophagus.

(Table 2). Since there were only 2 cases of adenocarcinoma of the oral cavity, pharynx, or esophagus among our subjects, we could not investigate the association between coffee consumption and this cancer. We excluded cases of oral, pharyngeal, or esophageal cancer diagnosed during the first 3 years of follow-up to avoid any possible bias resulting from the influence of undiagnosed oral, pharyngeal, or esophageal cancer present at baseline. In this analysis, 18 cases of cancer were excluded; however, the results did not essentially differ (data not shown).

Coffee consumption was also associated with a lower incidence risk of oral/pharyngeal cancer and of esophageal cancer (Table 3). The multivariate-adjusted hazard ratios for 1 or more cups of coffee per day compared with no consumption were 0.35 (95% CI: 0.16, 0.77; *P* for trend = 0.009) for oral/pharyngeal cancer and 0.60 (95% CI: 0.37, 0.97; *P* for trend = 0.05) for esophageal cancer. We observed similar trends for men and women separately, but they were not statistically significant (data not shown).

The results of our analysis of the association of coffee consumption with the incidence risk of oral, pharyngeal, and esophageal cancers combined and stratified by alcohol consumption and smoking status are shown in Table 4. We observed an inverse association between coffee consumption and the risk of oral, pharyngeal, and esophageal cancers, even in groups at high risk of these cancers. A lower risk of oral, pharyngeal, and esophageal cancers was associated with higher coffee consumption in both the never and the current drinker strata. The multivariate-adjusted hazard ratios for 1 or more cups of coffee per day compared with no consumption were 0.43 (95% CI: 0.13, 1.41; *P* for trend = 0.17) for nondrinkers and 0.49 (95% CI: 0.31, 0.77; *P* for trend = 0.004) for current drinkers. Similarly, we found inverse associations between coffee consumption and the

Table 3. Hazard Ratios and 95% Confidence Intervals of the Incidence of Cancer of the Oral Cavity/Pharynx and Esophagus According to Coffee Consumption, Miyagi, Japan, 1990–2003

	Coffee Consumption			*P* for Trend[a]
	Never	Occasionally	≥1 Cup/Day	
Oral cavity/pharynx				
No. of person-years	88,290	181,669	225,242	
No. of incident cases	17	18	13	
Multivariate-adjusted hazard ratio[b]	1.00	0.50	0.35	0.009
95% confidence interval	Reference	0.26, 0.99	0.16, 0.77	
Esophagus				
No. of person-years	88,282	181,647	225,209	
No. of incident cases	37	36	39	
Multivariate-adjusted hazard ratio[b]	1.00	0.56	0.60	0.05
95% confidence interval	Reference	0.35, 0.90	0.37, 0.97	

[a] *P* values were calculated by treating the coffee consumption category as a continuous variable and as 2-sided.

[b] Adjusted for age (in years), sex, body mass index (<18.5, 18.5–24.9, ≥25.0 kg/m^2), alcohol consumption (never, former drinker, current drinker of <45.6 g ethanol/day, current drinker of ≥45.6 g ethanol/day), cigarette smoking (never smoked, former smoker, current smoker of <20 cigarettes/day, current smoker of ≥20 cigarettes/day), consumption of vegetables and fruits (≤2 times/month, 1–2 times/week, 3–4 times/week, every day), and green tea consumption (<1 cup/day, 1–2 cups/day, 3–4 cups/day, ≥5 cups/day).

incidence of oral, pharyngeal, and esophageal cancers for both the never and the current smoker groups at baseline. The multivariate-adjusted hazard ratios for 1 or more cups of coffee per day compared with no consumption were 0.50 (95% CI: 0.14, 1.81; *P* for trend = 0.29) for nonsmokers and 0.49 (95% CI: 0.30, 0.79; *P* for trend = 0.008) for current smokers.

DISCUSSION

In a population-based, prospective cohort of Japanese that included 157 cases of oral, pharyngeal, and esophageal cancers, we observed an inverse association between coffee consumption and the incidence risk of these cancers. This inverse association was consistent regardless of sex and the site of the cancers, and it was observed for both nondrinkers or nonsmokers and current drinkers or smokers at baseline.

Although many studies have assessed the relation between coffee consumption and oral, pharyngeal, or esophageal cancers, their results have been inconsistent. Of 12 case-control studies, 4 supported an inverse association (9, 13, 18, 19), 2 showed an increased risk (especially for hot coffee) (16, 17), and the other 6 suggested no association (8, 10–12, 14, 15). To our knowledge, only 2 prospective studies have investigated this issue. One, conducted in Norway, found no association (20). In that study, among 16,555 subjects during 11.5 years of follow-up, only 53 cases of cancer were ascertained, whereas we documented 157 cases of oral, pharyngeal, or esophageal cancer. The other prospective study reported an inverse association between coffee consumption and the risk of cancer of the buccal cavity and pharynx. Compared with those for the lowest coffee consumption category, the relative risks for the highest category were 0.5 for men and 0.7 for women (21). This result was consistent with that of our study, although the risk of esophageal cancer was not investigated.

Our results may be explained by anticarcinogenic components of coffee (5–7). Specifically, caffeine may suppress the progression of quiescent (G0 phase) cells into the cell cycle by inhibiting cell growth signal-induced activation of cyclin-dependent kinase 4 (7). Cafestol and kahweol have been suggested to inhibit DNA damage induced by some procarcinogens such as 7,12-dimethylbenz[*a*]anthracene and aflatoxin B_1 (6). Cafestol and kahweol are 2 coffee-specific diterpenes present in considerable quantities in coffee beans, as well as in unfiltered beverages, which can be isolated from coffee oil (27).

A pooled analysis of 2 prospective Japanese cohort studies, 1 of which used the same cohort as ours, suggested that green tea consumption is associated with a significantly increased risk of esophageal cancer, and it was suggested that drinking the tea at high temperature might be involved (28). Furthermore, several other studies have suggested that drinking hot beverages is associated with an increased risk of cancers of the pharynx (17) and esophagus (3, 15, 16, 29). However, we observed an inverse association between coffee consumption and the risk of esophageal cancer. Although we did not ask our participants about the temperature at which they drank their coffee, our findings imply that some component or components of coffee have a strongly protective effect against these cancers that offsets the negative effect of drinking hot beverages.

One of the most significant findings of our study was that the inverse association between coffee consumption and the

Table 4. Hazard Ratios and 95% Confidence Intervals of the Incidence of Cancer of the Oral Cavity, Pharynx, and Esophagus Combined According to Coffee Consumption in Strata of Alcohol Consumption and Cigarette Smoking, Miyagi, Japan, 1990–2003

	Coffee Consumption			*P* for Trend[a]
	Never	Occasionally	≥1 Cup/Day	
Alcohol consumption				
Never				
No. of person-years	36,773	70,019	81,257	
No. of incident cases	8	11	5	
Multivariate-adjusted hazard ratio[b]	1.00	0.86	0.43	0.17
95% confidence interval	Reference	0.34, 2.19	0.13, 1.41	
Former drinker				
No. of person-years	4,846	7,755	10,742	
No. of incident cases	3	3	4	
Multivariate-adjusted hazard ratio[b]	1.00	0.74	0.91	0.93
95% confidence interval	Reference	0.15, 3.75	0.18, 4.51	
Current drinker				
No. of person-years	38,688	83,178	116,694	
No. of incident cases	41	35	41	
Multivariate-adjusted hazard ratio[b]	1.00	0.43	0.49	0.004
95% confidence interval	Reference	0.27, 0.68	0.31, 0.77	
Cigarette smoking				
Never				
No. of person-years	43,742	84,584	95,338	
No. of incident cases	7	9	4	
Multivariate-adjusted hazard ratio[c]	1.00	0.78	0.50	0.29
95% confidence interval	Reference	0.29, 2.13	0.14, 1.81	
Former smoker				
No. of person-years	10,404	18,842	20,075	
No. of incident cases	9	10	6	
Multivariate-adjusted hazard ratio[c]	1.00	0.65	0.51	0.21
95% confidence interval	Reference	0.26, 1.61	0.18, 1.47	
Current smoker				
No. of person-years	23,161	50,017	88,198	
No. of incident cases	36	28	40	
Multivariate-adjusted hazard ratio[c]	1.00	0.39	0.49	0.008
95% confidence interval	Reference	0.24, 0.65	0.30, 0.79	

[a] *P* values were calculated by treating the coffee consumption category as a continuous variable and as 2-sided.

[b] Adjusted for age (in years), sex, body mass index (<18.5, 18.5–24.9, ≥25.0 kg/m^2), cigarette smoking (never, former smoker, current smoker), consumption of vegetables and fruits (≤2 times/month, 1–2 times/week, 3–4 times/week, every day), green tea consumption (<1 cup/day, 1–2 cups/day, 3–4 cups/day, ≥5 cups/day).

[c] Adjusted for age (in years), sex, body mass index (<18.5, 18.5–24.9, ≥25.0 kg/m^2), alcohol consumption (never, former drinker, current drinker), consumption of vegetables and fruits (≤2 times/month, 1–2 times/week, 3–4 times/week, every day), green tea consumption (<1 cup/day, 1–2 cups/day, 3–4 cups/day, ≥5 cups/day).

risk of oral, pharyngeal, and esophageal cancers was consistent across the strata of sex and cancer site. Furthermore, the inverse association was also observed in populations with a high risk of these cancers, namely, those who were current drinkers and/or smokers at baseline.

The association of coffee consumption with cancer of the digestive organs, such as the stomach, pancreas, liver, and colorectum, has been investigated. Accumulated evidence now suggests that coffee consumption is associated with a decreased risk of liver cancer (30, 31) but has no association

with gastric cancer (32) or pancreatic cancer (33, 34). However, the issue of whether there is no, or an inverse, association between coffee consumption and colorectal cancer is still under discussion (35–38). Some of this evidence is inconsistent with our findings that coffee has a protective effect on oral, pharyngeal, and esophageal cancers. However, these differences could be interpreted in other ways. First, the effect of coffee consumption may be dependent on site-related differences in the histology of the cancer. Most gastric and colorectal cancers are adenocarcinomas, whereas oral, pharyngeal, and esophageal cancers are mainly squamous cell carcinomas. Indeed, more than 80% of the oral, pharyngeal, and esophageal cancers in our study population were squamous cell carcinomas. Second, before reaching the epithelium of the stomach and colorectum, some constituents of coffee may lose their anticarcinogenic effect because of exposure to digestive juices such as gastric or bile acids or pancreatic juice. In contrast, the epithelium of the oral cavity, pharynx, and esophagus is directly exposed to coffee that has not been affected by digestive juice.

Our study had several strengths. To our knowledge, it is the first prospective cohort study to focus on this issue. We used data on subjects from the general Japanese population and identified an adequate number of cases of oral, pharyngeal, and esophageal cancer (157 cases) over a long follow-up period (494,935 person-years). In addition, we carefully considered possible risk factors for oral, pharyngeal, and esophageal cancers as covariates in our estimations of multivariate-adjusted hazard ratios.

Our study also had some limitations. First, we collected information on coffee consumption only once, at baseline. Therefore, measurement error caused by changes in coffee consumption over time among the subjects could have distorted our results. Second, we excluded 7,780 subjects from our analysis because they incompletely answered, or did not answer, the question on coffee consumption. In this excluded group, 59 cases of oral, pharyngeal, or esophageal cancer (52 in men and 7 in women) were diagnosed. The multivariate-adjusted hazard ratio of oral, pharyngeal, or esophageal cancer in the subjects who did not report their coffee consumption ($n = 7,780$), compared with those who provided a complete report ($n = 38,679$), was not statistically significant (hazard ratio = 1.32, 95% CI: 0.93, 1.89; P for trend = 0.12). We also found that the baseline characteristics of the subjects who did not answer the question on coffee consumption were not different from those of subjects who did (data not shown). Therefore, our results were not substantially biased by exclusion of the subjects who did not answer the question on coffee consumption. Third, we did not investigate the form in which the coffee was consumed, such as whether it was filtered or boiled, caffeinated or decaffeinated. However, because boiled or decaffeinated coffee is not commonly consumed in Japan, most of the subjects would have drunk instant or filtered, caffeinated coffee (39).

We conclude that coffee consumption is related to a lower risk of oral, pharyngeal, and esophageal cancers in the general population of Japan. Although cessation of alcohol consumption and cigarette smoking is currently the best known way to help reduce the risk of developing these cancers, coffee could be a preventive factor in both low-risk and high-risk populations. Our results have pharmacologic implications for clinical medication of these cancers. Further studies to confirm the role of coffee in preventing these cancers are necessary.

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福井県におけるがん罹患と生存率の推移

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1. はじめに

福井県では昭和 59 年に県医師会主導による福井県悪性新生物実態調査を実施し、昭和 60 年からは福井県のがん登録事業に発展し、以降福井県医師会に委託して、毎年がん登録を実施している。今回昭和 59 年－平成 12 年の福井県におけるがんの罹患および死亡状況、昭和 59 年－平成 7 年の 5 年生存率の推移を検討した。

2. 対象と方法

福井県では生存率算出のために予後情報の収集として、次の 3 つのことを実施している。

(1) 医療機関からの届出を診断確定時と死亡時の 2 回収集する。

(2) 全死亡患者とマスターファイルの照合を行う。そのうちがんによる死亡に対しては補充票の収集を行う。

(3) 診断後 5 年経過した時点で予後情報の得られていない患者に対しては、市町村に依頼し住民票照会によって生死の確認を行う。

以上により追跡不能者は 3%前後であった。

乳がんと子宮がんは女性のみ、全部位とその他の部位は男女計の集計とした。年齢調整罹患率および死亡率の標準人口には世界人口を用いた。

3. 結果と考察

(1) 登録精度の推移

がん登録実施初期より高い登録精度を得るために、

① 登録事業を福井県医師会に委託し、福井県医師会長名での各医療機関への届出勧奨、

② 地域中核病院での病歴室の整備および院内がん登録の奨励、

③ 大学病院、病理診断機関への病理出張採録

などを実施して、死亡票のみで登録されたものの割合は 5%前後を維持している。今後地域がん診療拠点病院の整備を利用して、より精度の高いがん登録を目指していきたい。

(2) 罹患率の推移

全部位の年齢調整罹患率は平成 8－10 年に

表 1. 福井県がん登録の精度の推移　　昭和 59 年－平成 12 年

年	人口	悪性新生物		届出精度		診断精度			自主的届出
		罹患数	死亡数	DCO(%)	I / D	H / I(%)	H / R(%)	CH/ R(%)	登録率(%)
s59-s61	815,229	2,570	1,368	9.1	1.88	68.7	75.5	81.0	79.9
s62-h01	822,773	2,709	1,491	2.4	1.81	75.0	76.8	81.4	80.3
h02-h04	550,307	2,992	1,588	3.3	1.88	73.3	75.8	80.7	79.8
h05-h07	828,291	3,312	1,699	4.3	1.95	70.3	73.4	79.9	84.1
h08-h10	829,341	3,791	1,939	6.1	1.96	69.1	73.6	82.6	81.4
h11-h12	830,083	3,849	2,056	4.8	1.88	69.5	72.8	81.1	84.0

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は 226.2 まで増えたが平成 11－12 年には若干低下した。胃がんの罹患率は減少しているが、大腸がん、肺がん、乳がんの罹患率は増加している。子宮がんの罹患率は平成 2－4 年まで減少していたが、その後増加に転じた。

(3) 死亡率の推移

がんによる死亡数は年々増加傾向にあるが、年齢調整死亡率でみるとそれほど増加していない。胃がんの死亡率は罹患率同様に減少している。大腸がんの中でも結腸がんの死亡率は増加しているが、直腸がんの死亡率は減少している。肺がん、乳がんの死亡率は増加している。子宮がんの死亡率は平成 5－7 年まで減少していたが、その後増加している。

(4) 5 年生存率の推移

登録初期には 41.1%だった全部位の 5 年相対生存率も、次第に改善され最近では 47.1％となった。全部の主要部位で生存率の改善が認められるが、とくに結腸がんでは昭和 59－61 年 48.7 だったのが平成 5－7 年には 67.0 と 20%近い改善が認められた。集団検診が開始され、また全大腸内視鏡検査が普及し、早期がんが多く発見されるようになったことが大きな要素を占めていると考えられるが、今後進行度別の生存率の検討が必要と思われた。

表 2. 年齢調整罹患率の推移　昭和 59 年－平成 12 年

	s59-s61	s62-h01	h02-h04	h05-h07	h08-h10	h11-h12
全部位	199.1	194.1	201.7	210.8	226.2	215.4
胃	61.0	56.9	54.7	50.1	51.4	43.8
結腸	15.7	17.6	18.3	22.1	23.2	22.4
直腸	9.6	10.4	11.1	11.3	13.9	12.0
肝臓	11.3	12.5	13.4	14.8	14.7	14.4
胆嚢	8.4	8.4	8.1	8.2	8.2	7.4
膵臓	6.7	6.7	6.9	7.6	7.4	7.5
肺	18.7	18.7	13.7	21.2	23.6	23.3
乳房	23.7	21.6	29.0	31.8	32.9	37.4
子宮	18.8	16.1	14.5	17.7	17.6	18.0

表 3. 年齢調整死亡率の推移　昭和 59 年－平成 12 年

	s59-s61	s62-h01	h02-h04	h05-h07	h08-h10	h11-h12
全部位	99.0	97.4	100.3	94.9	99.9	96.9
胃	24.6	23.1	22.4	19.1	18.0	16.4
結腸	6.5	6.4	7.0	6.8	7.0	8.3
直腸	4.4	4.1	3.4	3.8	3.9	3.2
肝臓	9.4	9.9	10.1	10.7	11.1	10.5
胆嚢	6.0	6.4	6.9	6.3	5.9	5.8
膵臓	6.3	6.5	7.0	6.5	6.3	6.6
肺	14.9	15.8	17.5	15.9	18.1	17.7
乳房	4.3	4.3	4.5	6.3	7.8	6.7
子宮	4.7	4.4	3.4	2.8	2.9	3.2

表 4. 5 年相対生存率の推移　昭和 59 年－平成 7 年

	s59-s61	s62-h01	h02-h04	h05-h07
全部位	41.1	42.4	44.7	47.1
胃	51.3	54.3	54.2	57.6
結腸	48.7	56	60.4	67.0
直腸	51.7	51.5	59.7	60.6
肝臓	5.7	7.3	12.2	12.8
胆嚢	11.9	13.9	15.5	19.0
膵臓	3.4	3.2	2.8	6.2
肺	8.5	10.1	11.4	14.9
乳房	77.2	82.1	85.0	80.5
子宮	71.5	72.9	76.8	74.9

福井県における子宮がんの動向について

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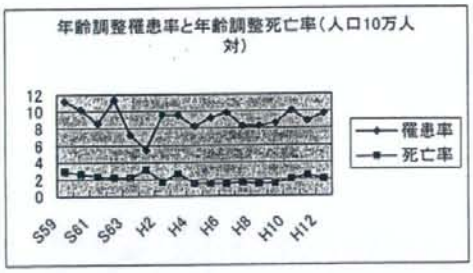
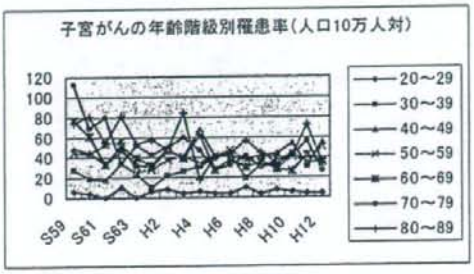
近年、がん死亡は増加傾向にあるが、子宮頸がんに関しては減少傾向である。しかし、性交年齢の低下に伴い若年者の子宮頸がんが問題となっている。子宮がん検診は昭和 57 年度より老人保健法に基づき、30 歳以上の婦人を対象に開始されているが、福井県ではそれに先駆けて昭和 47 年度より開始され、毎年約 1 万 7 千～2 万人の受診者がおり、5～7％の受診率となっている。地域がん登録、検診データを基に福井県の子宮がんの罹患率、罹患者の年齢階級別年次推移、子宮がんの来院経緯（検診群と病院群）による 5 年生存率の比較などを検討した。

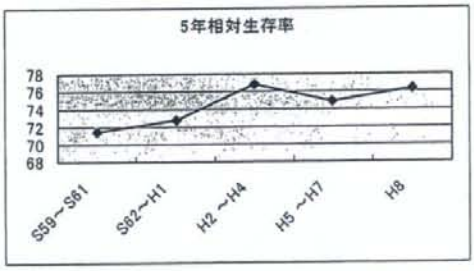


年齢調整罹患率は昭和 59 年から平成 12 年までに 0.87 倍、年齢調整死亡率は 0.69 倍と福井県でも減少していた。



昭和 59 年では第 1 位は 70 代、第 2 位は 60 代となっているが、平成 12 年では、第 1 位が 40 代、第 2 位が 50 代と若年化している。また、最近問題となっている若年者に関しては 30 代が増加傾向になっていた。

福井県での 5 年相対生存率は改善傾向であり、stage 別（Ⅰ、Ⅱ）、年齢別において病院受診群と検診受診群で比較したところ、有意差を認め、検診の効果を示すことができた。しかし、子宮がん検診受診者は全国と比較しても減少傾向にあり、近年子宮がん罹患率が増加傾向の若年者の受診者も減少傾向となっている。そこで、子宮がん検診受診者の増加、若年者の検診受診者の増加が今後の課題である。



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福井県におけるがん患者受療動態について

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1．はじめに

がんによる死亡を減少させるためには、がんの1次予防と同時に早期発見と質の高い医療が必要である。そのためには、がんの部位・特性を考慮しつつ、地域の拠点となるがん診療施設の適切な整備が効果的である。現在がん医療の均てん化を推進するためにがん診療病院の整備が進められているが、その資料としてがん患者の受療動態の特性を知る必要がある。福井県がん登録資料に基づき、患者居住地と主治療機関の所在地との関係、がん診療拠点病院と福井県がん医療との関係を比較検討した。

2．対象と方法

福井県地域がん登録資料に基づき受療動態は2000-2002年に、5年生存率は1994-1998年に初めてがんと診断された患者で、DCO症例を除いた例を対象とした。受療動態の対象者には上皮内がん患者を含み、5年生存率の算出には上皮内がんおよび大腸の粘膜内がん患者は除いた。主治療機関の判断は、手術、放射線療法、化学療法の順に優先し目視で行った。

3．結果

福井県は保健医療計画区分によって福坂地域、奥越地域、丹南地域、嶺南地域の4つの2次医療圏に分けられている。2000年の福井県の人口は828,944人で、福坂地域402,106人、奥越地域67,775人、丹南地域206,578人，嶺南地域154,485人だった。福井県ではがん診療拠点病院として5病院が認定されたが、そのうち4病院が福坂地域、1病院が嶺南地域に存在し、奥越地域と丹南地域にはがん診療拠点病院がなく福坂地域の2つの病院が担当している。

福坂地域のがん患者5,571例は大部分が福坂地域内の医療機関で治療を受けていたが、奥越地域は約80%、丹南地域は約70%、

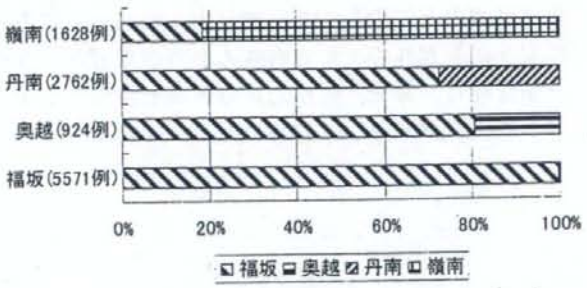

図1　患者居住地別治療地域

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