Increase in incidental detection of thyroid cancer in Osaka, Japan

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Using Osaka Cancer Registry data, we examined age-specific and age-adjusted incidence rates of thyroid cancer according to the route of thyroid cancer detection from 1992 to 2012. The detection routes were categorized into "symptomatic" and "incidental detection." Age-specific incidence rates of incidentally-detected thyroid cancer consistently increased during the study period, especially after 2001, for all sex and age groups other than childhood. The rate of symptomatic thyroid cancer did not largely differ among groups. Age-adjusted incidence rates of symptomatic thyroid cancer were around 1.5 and 4.5 per 100 000 among men and women, respectively. The rate of incidentally-detected thyroid cancer increased from 0.1 and 0.1 per 100 000 person-years among men and women in 1992-1994 to 2.0 and 4.9, respectively, in 2010-2012. Age-adjusted mortality rates among both sexes during the study period leveled off. This finding suggests that the thyroid cancer incidence rate in Osaka increased with incidental detection. We need to continue careful monitoring to confirm these findings.

KEYWORDS
incidental cancer, incidental detection, overdiagnosis, thyroid cancer, thyroid cancer incidence

1 | INTRODUCTION

Several studies have reported a worldwide increase in thyroid cancer incidence and a decreasing trend in mortality. In Japan, the age-adjusted thyroid cancer incidence rate increased: from 2.1 and 9.3 per 100 000 person-years among men and women, respectively, in 1990 to 4.1 and 12.3 per 100 000 person-years in 2012. In contrast, the age-adjusted mortality rate slightly decreased: from 0.4 and 0.6 per 100 000 person-years among men and women, respectively, in 1990 to 0.3 and 0.4 per 100 000 person-years in 2012. The main cause of the increase in thyroid cancer in the US was assumed to be the detection and the diagnosis of small thyroid cancers. The advance of computer tomography, ultrasonography and fine needle aspiration cytology has made it possible to detect small thyroid cancers. In order to discuss the cause of the increase in thyroid cancer in Japan, we examined the thyroid cancer incidence rate according to the route of cancer detection using population-based cancer registry data for Japan.

2 | MATERIALS AND METHODS

The Osaka Cancer Registry (OCR), which was established in 1962, is a population-based cancer registry that covers the Osaka Prefecture (population: 8.8 million [2015 census]). Using OCR data on thyroid cancer incidence (International Classification of Diseases, 10th revision; C73) for cases diagnosed between 1992 and 2012, we calculated the age-specific incidence for each 3-year period, the age-specific incidence rate, the age-adjusted incidence rate according to the route of cancer detection and the age-adjusted mortality rate.
addition, we compared the age-adjusted incidence rate and age-adjusted mortality rate in Osaka with those for the whole of Japan. The mortality rate data and incidence data for the whole of Japan were obtained from Vital Statistics Japan\(^7\) and the Cancer Information Service of National Cancer Center, Japan.\(^8\)

In the OCR data, the route of cancer detection is classified as 1 of the following 5 categories: (i) cancer screening; (ii) health checkup; (iii) incidental detection during follow up of another disease; (iv) autopsy; and (v) other. Cases detected from symptoms assumed to be relevant to the cancer were categorized as "other." Incidentally-detected cases were categorized to the previous 4 categories. In the present study, we defined the route of cancer detection as either "incidentally detected" or "symptomatic." Cases detected by autopsy and cases with routes missing were excluded from the analysis. Cases detected by cancer screening, health checkup and follow up of another disease were defined as "incidentally detected." The others were defined as "symptomatic." The incident years were divided into 3-year time periods: 1992-1994, 1995-1997 and 2010-2012. There were 4 age groups: 0-19, 20-44, 45-64 and 65 years or over. The population data by age group in Osaka Prefecture were obtained from the Population Census. For age-standardization (direct method), the Japanese model population in 1985 was used.

The statistical software package IBM SPSS Statistics 23.0 for Windows (IBM Japan, Tokyo, Japan) was used to tabulate the number and rate of thyroid cancer incidence and mortality. This study was exempt from institutional ethical review because patient information could not be identified from the data.

### 3 RESULTS

A total of 10 426 thyroid cancer cases were registered in OCR. Of these, 442 cases for which the route of cancer detection was missing and 107 cases detected from autopsy were excluded from the analysis. The remaining 9877 cases were enrolled in the present study.

Table 1 shows the trends in age-specific thyroid cancer incidence and the incidence rate for each 3-year period according to the route of cancer detection. Thyroid cancer incidence among both men and women increased constantly during the study period. The proportion of incidentally-detected cancer increased rapidly from 1998-2000 and reached 57.5% among men and 50.6% among women in 2010-2012. This increasing tendency was notable in the elderly: from 0% for both men and women aged 65 years or over in 1992-1994 to 53.6% for men and 46.1% for women in 2010-2012. In contrast, the incidence in childhood among both males and females was very low and changed little.

The age-specific incidence rate of symptomatic thyroid cancer leveled off during the study period for all sex and age groups. In contrast, the rate of incidentally-detected thyroid cancer increased rapidly for all sex and age groups other than childhood. The rate of incidentally-detected thyroid cancer for men and women aged 45-64 overtook the rate of symptomatic thyroid cancer in 2007-2009.

### 4 DISCUSSION

The present study is the first report to examine trends in the incidence rate of thyroid cancer according to the route of cancer detection in Japan. The age-specific and age-adjusted incidence rates of thyroid cancer both increased. However, the incidence rate of symptomatic thyroid cancer did not differ during the study period. The proportion of incidentally-detected thyroid cancer increased and reached approximately half in 2010-2012.

In the USA, some studies have reported that the age-adjusted incidence rate of thyroid cancer increased due to the detection of small thyroid cancers.\(^4\)-\(^6\),\(^9\) The incidence rate of small papillary thyroid carcinomas, sized 2.0 cm or under, has increased twofold since the 1990s, while that of large papillary carcinoma, sized 2.1 cm or over, has almost leveled off.\(^5\)

As information on tumor size was unavailable for the present study, we focused on the route of cancer detection instead. Symptoms of thyroid cancer, neck mass, dysphagia, orthopnea and hoarseness would generally be seen in large cancers.\(^5\) Because most incidentally-detected thyroid cancers would not have subjective symptoms, incidentally-detected thyroid cancers would tend to present as small thyroid cancers.

Population-based thyroid cancer screening has not been introduced in Japan. Our findings suggest that in Japan incidental detection is due to opportunistic cancer screening, health checkups and follow ups of other diseases using computer tomography, carotid or thyroid ultrasonography. Ultrasonography and fine needle aspiration cytology have the potential to diagnose small thyroid cancers measuring a minimum of 3.0 mm.\(^10\) The increase in incidentally-detected thyroid cancer in the present study might be due to the increase in exposure to medical tests.

In contrast, age-adjusted mortality in the USA increased slightly. This increase in mortality might be a result of various factors, not only the detection of small thyroid cancers but also X-rays, iodine intake, thyroiditis, obesity and environmental pollutants.\(^3\),\(^5\) In Osaka, age-adjusted mortality from thyroid cancer during the study period leveled off: around 0.5 and 0.8 per 100 000 person-years among men and women. Various factors would affect
**TABLE 1** Trends in age-specific thyroid cancer incidence and incidence rate per 100,000 person-years for each 3-year period according to the route of cancer detection (N = 9877)*

| Route of cancer detection | Incident year | 1992-1994 | 1995-1997 | 1998-2000 | 2001-2003 | 2004-2006 | 2007-2009 | 2010-2012 |
|---------------------------|--------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| **Men**                   |              |           |           |           |           |           |           |           |
| **Age**                   |              |           |           |           |           |           |           |           |
| 0-19                      | Symptomatic  | Number    | 2         | 3         | 2         | 3         | 4         | 4         | 1         |
|                           |              | Incidence rate | 0.1      | 0.1       | 0.1       | 0.2       | 0.2       | 0.0       |           |
|                           | Incidentally detected | Number | 0         | 0         | 1         | 1         | 0         | 0         | 2         |
|                           |              | Incidence rate | 0.0      | 0.0       | 0.0       | 0.0       | 0.0       | 0.1       | 0.0       |
|                           | Total        | Number    | 2         | 3         | 3         | 3         | 4         | 6         | 1         |
|                           |              | Incidence rate | 0.1      | 0.1       | 0.1       | 0.2       | 0.2       | 0.0       |           |
| 20-44                     | Symptomatic  | Number    | 28        | 36        | 38        | 30        | 41        | 54        | 33        |
|                           |              | Incidence rate | 0.6      | 0.7       | 0.8       | 0.6       | 0.9       | 1.2       | 0.8       |
|                           | Incidentally detected | Number | 2         | 2         | 3         | 3         | 5         | 16        | 42        |
|                           |              | Incidence rate | 0.0      | 0.0       | 0.1       | 0.1       | 0.4       | 0.9       | 0.8       |
|                           | Total        | Number    | 30        | 38        | 41        | 35        | 57        | 96        | 69        |
|                           |              | Incidence rate | 0.6      | 0.8       | 0.9       | 0.8       | 1.3       | 2.2       | 1.6       |
| 45-64                     | Symptomatic  | Number    | 93        | 93        | 103       | 104       | 88        | 95        | 99        |
|                           |              | Incidence rate | 2.5      | 2.4       | 2.7       | 2.8       | 2.5       | 2.8       | 3.0       |
|                           | Incidentally detected | Number | 6         | 3         | 8         | 11        | 52        | 113       | 169       |
|                           |              | Incidence rate | 0.2      | 0.1       | 0.2       | 0.3       | 1.5       | 3.3       | 5.1       |
|                           | Total        | Number    | 99        | 96        | 111       | 115       | 140       | 208       | 268       |
|                           |              | Incidence rate | 2.7      | 2.5       | 2.9       | 3.1       | 4.0       | 6.1       | 8.0       |
| 65+                       | Symptomatic  | Number    | 52        | 74        | 92        | 100       | 125       | 121       | 129       |
|                           |              | Incidence rate | 4.5      | 5.4       | 5.8       | 5.4       | 5.9       | 5.1       | 4.9       |
|                           | Incidentally detected | Number | 0         | 0         | 1         | 6         | 11        | 44        | 108       |
|                           |              | Incidence rate | 0.0      | 0.1       | 0.4       | 0.6       | 2.1       | 4.5       | 5.6       |
|                           | Total        | Number    | 52        | 75        | 98        | 111       | 169       | 229       | 278       |
|                           |              | Incidence rate | 4.5      | 5.5       | 6.1       | 6.0       | 8.0       | 9.6       | 10.5      |
| All                       | Symptomatic  | Number    | 175       | 206       | 235       | 237       | 258       | 274       | 262       |
|                           | Incidentally detected | Number | 8         | 6         | 18        | 27        | 112       | 265       | 354       |
|                           | Total        | Number    | 183       | 212       | 253       | 264       | 370       | 539       | 616       |
| **Women**                 |              |           |           |           |           |           |           |           |
| **Age**                   |              |           |           |           |           |           |           |           |
| 0-19                      | Symptomatic  | Number    | 10        | 9         | 8         | 5         | 11        | 8         | 5         |
|                           |              | Incidence rate | 0.3      | 0.3       | 0.3       | 0.2       | 0.5       | 0.3       | 0.2       |
|                           | Incidentally detected | Number | 0         | 0         | 0         | 0         | 1         | 4         | 3         |
|                           |              | Incidence rate | 0.0      | 0.0       | 0.0       | 0.0       | 0.2       | 0.1       | 0.2       |
|                           | Total        | Number    | 10        | 9         | 8         | 6         | 15        | 11        | 10        |
|                           |              | Incidence rate | 0.3      | 0.3       | 0.3       | 0.2       | 0.6       | 0.5       | 0.4       |
| 20-44                     | Symptomatic  | Number    | 140       | 142       | 129       | 116       | 115       | 136       | 160       |
|                           |              | Incidence rate | 2.9      | 3.0       | 2.7       | 2.5       | 2.5       | 3.0       | 3.6       |
|                           | Incidentally detected | Number | 7         | 6         | 5         | 13        | 64        | 136       | 172       |
|                           |              | Incidence rate | 0.1      | 0.1       | 0.1       | 0.3       | 1.4       | 3.0       | 3.9       |
|                           | Total        | Number    | 147       | 148       | 134       | 129       | 179       | 272       | 332       |
|                           |              | Incidence rate | 3.0      | 3.1       | 2.8       | 2.8       | 3.9       | 6.0       | 7.6       |

(Continues)
this trend. Although we need to interpret these findings with care, incidentally-detected thyroid cancer also has the potential for excess detection. In Korea, opportunistic thyroid cancer screening using ultrasonography increased from the 2000s. As a result, a rapid rise in the thyroid cancer incidence rate occurred, while the mortality of thyroid cancer leveled off.2,11 Thus, it appears that excessive medical checks for thyroid can lead to excess detection.

The increasing trend of incidentally-detected thyroid cancer was more gradual for the younger age group and was not detected in childhood. This finding may be reasonable because young people generally have fewer opportunities to undergo medical tests than the elderly.

The present study has several limitations. First, the completeness of the registry for thyroid cancer in the OCR was not perfect,
although the proportion of death certificate only (DCO), which is often regarded as an index of completeness, was low, at approximately 2.9% in 2012. Second, because we used data from the OCR, we need to interpret the findings with limited generalizability to the whole of Japan. Although the age-adjusted mortality of thyroid cancer in Osaka was almost equal to that for the whole of Japan, the age-adjusted incidence rate of thyroid cancer in Osaka was slightly lower than that for the whole of Japan. This trend was constant from the 1990s, when incidentally detected thyroid cancer was relatively rare.

Third, there may be misclassification in the route of thyroid cancer detection. Symptoms are not always relevant with thyroid cancer. General symptoms of thyroid cancer are neck mass and/or hoarseness. However, some cases might take diagnostic imaging of neck by non-relevant symptom with thyroid cancer. As there is a possibility that cases detected by symptoms unrelated to thyroid cancer were classified as “symptomatic,” the estimated symptomatic thyroid cancer incidence might be higher than the actual figure.

In conclusion, we described trends in thyroid cancer incidence according to detection route using population-based data from a cancer registry in Japan. An increase in incidentally-detected thyroid cancer was observed, partly suggesting overdiagnosis. Careful monitoring is necessary to confirm these findings.

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CONFLICT OF INTEREST

We have no conflicts of interest to declare.

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