



Management of incidental anterior mediastinal lesions: summary of relevant studies

Soon Ho Yoon

Department of Radiology, Seoul National University Hospital, Seoul National College of Medicine, Seoul, Korea

Correspondence to: Soon Ho Yoon, MD, PhD. Department of Radiology, Seoul National University Hospital, 101, Daehangno, Jongno-gu, Seoul 110-744, Korea. Email: yskoka@gmail.com.

Abstract: With the increasing use of chest computed tomography (CT) imaging, the detection of asymptomatic incidental lesions in the anterior mediastinum has become more frequent. The prevalence of incidental nodular lesions in the anterior mediastinum is 0.49% to 0.89%. Most of these lesions manifest as soft tissue nodules measuring between 10 and 30 mm on non-contrast CT images. Thymic epithelial tumors are mainly responsible for larger lesions, while smaller lesions are primarily benign cysts. Most incidental thymic epithelial tumors are early-stage and have a favorable outcome. During follow-up, most lesions are stable, but some show indolent growth. Incidental lesions can be managed by a conservative patient-tailored approach with regular follow-up and the use of non-invasive imaging modalities such as magnetic resonance imaging.

Keywords: Anterior mediastinum; thymus; computed tomography (CT)

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Mediastinal lesions include a variety of benign and malignant diseases. Half of these lesions are located in the anterior mediastinum, mostly originating from the thymus (1). With the increasing use of chest computed tomography (CT) imaging in clinical practice (2) and lung cancer screening (3), asymptomatic incidental anterior mediastinal lesions are more frequently encountered. Three studies have dealt with the prevalence of incidental nodular lesions in the anterior mediastinum (4-6) (Table 1). The first was from the Early Lung Cancer Action Project (ELCAP) (4), the second utilized data from the Framingham Heart Study (5), and the third was conducted at two health checkup centers affiliated with a tertiary academic hospital (6). The number of participants ranged from 2,571 to 56,358, and the age and sex distribution was similar across the studies. However, ever-smokers were more prevalent in the ELCAP study (4) than in the others (5,6). Most participants in the three studies underwent thin-slice CT scans (1.25 mm or thinner), but in the ELCAP study (4), the slice thickness was 2.5 or 10 mm in the baseline CT images of 32% of the participants.

The prevalence of incidental nodular lesions in the anterior mediastinum in these studies ranged from 0.45% to 0.89% (Table 1). The ELCAP study reported a prevalence of 0.45% (95% CI, 0.32–0.60%; 41 of 9,263 participants) (4). The Framingham Heart Study reported a prevalence of 0.89% (95% CI, 0.59–1.35%; 23 of 2,571 participants) (5). Lastly, among 56,358 healthy participants who underwent a low-dose chest CT scan as part of their health checkups, the prevalence was 0.73% (6). The variation in the prevalence across these studies seems to have been due to differences in the study population, CT slice thickness, and lesion definition. The ELCAP study (4) applied a cutoff of a short-axis diameter of 7 mm or larger to identify incidental nodular lesions, whereas the other two studies (5,6) adopted a cut-off of 5 mm or larger.

One study (6) reported that the prevalence of incidental lesions increased with age, with the following distribution: 25–34 years, 0.40%; 35–44 years, 0.47%; 45–54 years, 0.58%; 55–64 years, 0.89%; 65–74 years, 1.26%; >75 years, 1.44% ($P < 0.001$). The prevalence of incidental lesions was not associated with sex, cigarette smoking, or body

Table 1 Baseline characteristics of relevant studies on incidental lesions in the anterior mediastinal mediastinum

Source	Study from the Early Lung Cancer Action Project	Study from the Framingham Heart Study	Study conducted at two health checkups centers
Study location	United States	United States	South Korea
Study period	1993–2003	2008–2011	2006–2013
Number of participants	9,263	2,571	56,358
Median age	65 years	59 years	52 years
Sex (M, F)	49%, 51%	49%, 51%	54%, 46%
Proportion of ever-smoking	100%	51%	57%
Slice thickness of baseline computed tomographic images	1.25 mm (68%), 2.5 or 10 mm (32%)	0.6 mm	1 mm

Table 2 Prevalence and computed tomographic findings of incidental lesions in the anterior mediastinal mediastinum

Source	Study from the Early Lung Cancer Action Project	Study from the Framingham Heart Study	Study conducted at two health checkups centers
Size cutoff for defining incidental lesions*	≥7 mm	≥5 mm	≥5 mm
Number of incidental lesions	41	23	413
Prevalence (95% confidence interval)	0.45% (0.32–0.60%)	0.89% (0.59–1.35%)	0.73% (0.66–0.80%)
Computed tomographic findings			
Median long-axis diameter (mm)	Between 10 and 30	18 [11–30]*	12 [9–16]*
Median short-axis diameter (mm)	Unknown	11 [7–14]*	8 [6–10]*
Attenuation (Hounsfield units)	Unknown	32 [10–56]*	43 [26–57]*
Round to oval shape	95%	68%	99%
Focal calcification	5%	9%	Unknown

*, Data in parentheses indicate interquartile range.

mass index (5,6). Patients with a history of malignancy had incidental lesions more frequently than those with no such history (2.06% versus 0.72%; $P=0.005$) (6). A similar tendency of the increased thymoma risk following other malignancies was found in the SEER data (standardized incidence ratio, 1.3; 95% CI, 1.0–1.7), despite the lack of significant association between particular cancer and thymoma (7).

Most incidentally-detected lesions in the anterior mediastinum were small nodules with a soft tissue appearance (Table 2). The long-axis diameter of the lesions was mostly between 10 and 30 mm (4), with a median value of 12 to 18 mm (5,6). The shape of the lesions was typically round to oval. The mean CT attenuation of the lesions was 32 to 43 Hounsfield units (5,6), which corresponds to soft tissue attenuation. Focal calcifications within the

lesions were rare (4,5). In other words, most lesions had CT features indistinguishable from those of thymic epithelial tumors on precontrast CT images.

The distribution of pathologies in anterior mediastinal lesions varies according to age and sex (8). Because incidental anterior mediastinal lesions are primarily encountered on screening chest CT scans in patients in their 50–70 s, thymic epithelial tumors are a main concern. Malignant lesions seem to be more prevalent among larger lesions in the anterior mediastinum, especially among those measuring 30 mm or larger. More specifically, thymic epithelial tumors are mainly responsible for larger lesions, whereas smaller lesions are primarily benign thymic cysts (Table 3). In two of the three studies, a small subset of the detected lesions (12% in each study) underwent surgical resection (4,6). In the ELCAP study (4), all five lesions

Table 3 Malignancy rates and results of follow-up of incidental lesions in the anterior mediastinal mediastinum

Source	Study from the Early Lung Cancer Action Project	Study from the Framingham Heart Study	Study conducted at two health checkups centers
Proportion of resection	12% (5/41)	0% (0/23)	12% (51/413)
Median long-axis diameter	>30 mm	Unknown	17 mm
Malignancy rate	80% (4/5)	Unknown	23% (12/51)
Proportion of observation	88% (36/41)	100% (23/23)	88% (362/413)
Proportion of lesions with follow-up	72% (26/36)	34% (8/23)	65% (237/362)
Median follow-up interval	1 year	6.5 years	4.2 years
Results of follow-up			
Proportion of growing lesions	19% (5/26)	75% (6/8)	9% (21/237)
Proportion of stable lesions	69% (18/26)	25% (2/8)	82% (195/237)
Proportion of shrinking lesions	12% (3/26)	0% (0/8)	9% (21/237)

larger than 30 mm were resected, and four of those lesions were malignant (proportion of malignancy, 80%), including three thymomas and one thymic carcinoma. The benign lesion was a thymic cyst. In contrast, in the study conducted at health checkup centers (6), 51 lesions were resected, of which 12 were malignant (proportion of malignancy, 23%): 11 thymic epithelial tumors and one case of non-small cell lung cancer. Among the 39 cases of benign disease, most were benign cysts in the thymic bed, including 32 thymic cysts and four bronchogenic cysts. The median long-axis diameter of the resected lesions was 17 mm. The discrepancy in the proportion of malignancy between the two studies may have been due to the different diameter of the resected lesions. Indeed, a subgroup analysis in the latter study showed that the proportion of malignancy was much higher in lesions larger than 20 mm than in those 20 mm or smaller (50% versus 13.5%; $P=0.011$).

Incidentally-detected thymic epithelial tumors had favorable outcomes when resected. One study (6) provided the detailed characteristics of the resected thymic epithelial tumors in 11 cases with a median long-axis diameter of 21 mm. Of the 11 resected thymic epithelial tumors, five were thymic carcinomas, 10 were stage I or II according to the Masaoka-Koga staging system, and all the lesions were completely resected without recurrence during a median follow-up of 5.6 years. Despite the small number of cases, the lack of recurrence of the incidental lesions is strikingly different from the recurrence rates of 11–13% that have been reported for clinically-detected thymic epithelial tumors (9), with a particularly higher recurrence rate for

thymic carcinoma (10).

In the study conducted at health checkup centers (6), 12% of the detected lesions were resected, resulting in a prevalence of thymic epithelial tumors (0.02%) that was twice as high (standardized prevalence ratio, 2.04) as the expected prevalence (0.01%) based on national cancer statistics. Indeed, incidental thymic epithelial tumors seem fairly prevalent. A postmortem study also reported a higher prevalence of thymic epithelial tumors (0.18%; 57 of 31,000) than would be predicted based on the national cancer statistics (11). It remains unclear whether the surgical resection of incidental thymic epithelial tumors leads to overdiagnosis or whether the resection of the lesions results in a survival benefit in patients with thymic epithelial tumors.

In all three studies (4–6), 88–100% of the incidentally detected lesions were managed by close observation with follow-up CT scans, although the proportion of patients receiving follow-up and the follow-up interval were inhomogeneous across the studies (*Table 3*). A majority of the incidental lesions were stable during follow-up (4,6), except for the study based on the Framingham Heart Study (5), which reported a growth in 75% of lesions over a longer follow-up of 6.5 years. Nevertheless, even in the latter study, the growing lesions measured approximately 30 mm on the follow-up CT scans (median long-axis diameter, 27 mm; range, 10–38 mm). The median follow-up duration to notice an increase was quite long (3.7 years) and the median increase of the longest diameter was 3 mm (6). Thus, incidental lesions seem mostly stable; some lesions do grow

over multi-year follow-up, but their growth is indolent.

Conservative management with follow-up is recommended for incidental lesions. Nevertheless, regular follow-up may not be the sole solution, as long-term repeated follow-up is required to detect any increase or decrease in lesion size and neither interval growth nor a lack of growth during follow-up can guarantee either malignancy or benignity (6). Non-invasive imaging studies such as thoracic magnetic resonance imaging (MRI) can be helpful for further characterizing incidental anterior mediastinal lesions, especially thymic cysts (12), and for alleviating patients' anxiety. Indeed, state-of-art thoracic MRI offers excellent contrast resolution, which enables various tissue characteristics of anterior mediastinal lesions to be depicted without motion artifacts (13).

In conclusion, the prevalence of incidental anterior mediastinal lesions ranges from 0.45% to 0.89%, and many of these lesions are suspected to be benign. A conservative patient-tailored approach with follow-up is required, and thoracic MRI can be used as a supplementary tool for the management of the lesions.

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