Editorial

Is there any consensus of long-term follow-up for incidental anterior mediastinal nodular lesions?

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With the recent increase of computed tomography (CT) examination, the detection of mediastinal nodular lesions is becoming more common. According to previous reports, approximately two thirds of mediastinal nodules/masses are benign, and this increases to three fourths among asymptomatic patients (1). About half of these nodules/masses are located in the anterior mediastinum (prevascular compartment) (2-4). Thymic epithelial tumors (TETs), including thymomas, thymic carcinomas, and thymic neuroendocrine tumors are extremely important types of thymic tumors, based on the World Health Organization classification. Among these, thymoma is the most frequent type of tumor, accounting for approximately 40–50% of anterior mediastinal masses and 80% of all TETs (2-4). Thymic carcinoma and thymic neuroendocrine tumors are cytologically and clinically malignant tumors, accounting for approximately 15–20% and 2.5% of all TETs, respectively (2). Mediastinal germ cell tumors (GCTs) and malignant lymphoma account for approximately 10–26% and 7–17% of anterior mediastinal masses, respectively (4).

There are several previous reports that analyzed the frequency and follow-up method for anterior mediastinal masses (5,6) or suggested approaches for these masses for radiologists (7) and clinicians (8). However, the management of incidental anterior mediastinal masses remains unclear. It is important to be aware of the frequency and management of incidental mediastinal masses, which are detected by screening CT examination, in asymptomatic patients to reduce unnecessary examination.

The recent study by Yoon and colleagues (9) analyzed the prevalence of anterior mediastinal nodular lesions on health checkup CT images. This is a well-written and clearly structured article. They mentioned differences in the prevalence of incidental anterior mediastinal nodular lesions between two previous studies. One study investigated the prevalence and incidence of mediastinal masses using screening CT images of high-risk participants for lung cancer in the Early Lung Cancer Project (ELCAP) (9,263 participants; median age, 65 years; range, 40–92 years; women, 51%), and reported that the prevalence of anterior mediastinal masses was 0.43% (5). The other study was the analysis of the prevalence and CT image characteristics of anterior mediastinal masses using cardiac CT scans of participants at high-risk for cardiovascular diseases in the Framingham Heart Study (2,571 participants; median age, 58.9 years; range, 34–92 years; women, 51%), and reported the prevalence of anterior mediastinal masses was 0.89% (6). Although these prevalence rates were quite different, several reasons may explain this, including the selection of participants, the types of anterior mediastinal masses, the size criteria, the CT scan technique, and the follow-up period.

The ELCAP study reported that the prevalence of mediastinal masses was 0.77% (71 of 9,263 participants), and 40 of these masses were located in the anterior mediastinum (39 thymic masses and one pericardial cyst). The prevalence of thymic masses was 0.45% (41 of 9,263 participants, 39 located in the anterior mediastinum,

and two located in the superior mediastinum). They excluded lymph node enlargement (5). The Framingham Heart Study (6) reported that the prevalence of anterior mediastinal masses was 0.89% (23 of 2,571 participants). Although none of the masses had been resected, the prevalence included not only thymic tumors but also other lesions (five solitary lymph nodes, two pericardial cysts, and two cases of thymic hyperplasia) (6). Hence, the types of masses included in each investigation were different.

In the ELCAP study, they considered mases as thymic masses if the short-axis measurement were >13 mm among bi-lobed and arrowhead shape masses, or ovoid shape masses with the short-axis measurements >7 mm. In addition, their study was based on long-term investigations and might have included CT images with a greater slice thickness (5). On the other hand, in the Framingham Heart Study, the anterior mediastinal mass was defined as a mass with a short axis diameter ≥5 mm using 3 mm or thinner sliced CT images (6). These factors suggest that the cases included in the ELCAP were limited compared with those of the Framingham Heart Study.

According to the ELCAP study (5), 39 of 41 thymic masses were ovoid shape, and five of these masses were >3.0 cm (one thymic cyst, three noninvasive thymomas, one thymic carcinoma). One of the noninvasive thymomas increased in size over 3 years follow-up. Among the rest of the 34 masses with ovoid shapes, 25 masses were evaluated at the 1-year follow-up, and most remained unchanged in size one year later (18 were unchanged, five were increased, and two were decreased in size). They recommended a mass resection when the thymic masses were >3.0 cm in diameter, and reported that it was no adverse effect from waiting at least one year for invasive procedures when the thymic masses <3.0 cm, even though the long-term management is unclear (5). In contrast, none of the anterior masses in the Framingham Heart Study were resected, and eight of 23 masses that could be assessed in previous CT images were followed for more than 5 years, and six of these increased in size more than 20% in the longest diameter even if the prior size was <3.0 cm (6).

The recent study by Yoon and colleagues (9) reported that the prevalence of incidental anterior mediastinal nodular lesions was 0.73% (413 of 56,358 participants) in a large population (mean age 52.4±10.5 years, range 40–92 years, 37.4% women). They investigated using CT at health checkups, resulting in less bias with the participants and a better survey of the general population. They included anterior mediastinal nodular lesions with a short axis diameter ≥5 mm, excluded lesions with typical CT features such as thymic remnant, thymic hyperplasia, triangular or quadrilateral shape soft tissue lesions containing fat attenuation in the center of the thymic bed, intrathoracic goiter, and soft tissue lesions retaining a connection with the thyroid gland.

Most of the nodular lesions (85.2%, 352 of 413) had a long axis diameter <2.0 cm, 10.4% (43 of 413) had diameters between 2.0 and 2.9 cm, 4.5% (18 of 413) between 3.0 cm and larger, and 61.3% had a round shape (the ratio of the long to the short axis was <1.5). Fifty of 413 nodular lesions were resected (six thymomas, five thymic carcinomas, one non-small cell lung cancer, 32 thymic cysts, four bronchogenic cysts, one teratoma, and one thymolipoma). Although the reason for the resection was unknown, malignant lesions accounted for 50% of the nodules >2.0 cm and 13.5% of those ≤2.0 cm. Among the subjects with these resected lesions, 21 of 50 (three thymomas, three thymic carcinomas, 14 thymic cysts, and one teratoma) underwent a follow-up CT scan before resection (median 25 months), and 10 of these nodules (two thymomas, three thymic carcinomas, and five thymic cysts) were increased in size. Conversely, 27 thymic cysts were resected, although it was not necessary.

As described in the discussion of the recent study by Yoon and colleagues (9), most of the nodule lesions had CT features that were indistinguishable from those of TETs, despite that TETs tend to increase in size. It is unclear if they examined using contrast-enhanced CT scan before the resection, although, this might be helpful to distinguish cystic lesions from solid lesions. It is well known that the cystic lesions of the mediastinum tend to show higher CT number values (HU) than water (zero HU) because of hemorrhage or protein-rich contents, and MR images of thymic cysts have been useful in the diagnosis (10). Although contrast-enhanced CT and MR images are helpful for the diagnosis of mediastinal masses, they should not be used for all masses, and excessive examination should be avoided.

As described previously, the ELCAP study reported that masses <3.0 cm should be followed up for at least one year (5). Nevertheless, in the Framingham Heart Study, the masses <3.0 cm increased in size during more than 5 years of follow-up (6). Yoon and colleagues reported that 65.6% of pathologically unconfirmed cases had a follow-up CT scan (median 50.9 months), and among these cases, 82.2% were stable, 8.9% increased (median time to increase 44.5 months), and the rest (8.9%) decreased in size (median time to decrease 34.7 months) (9). The definition of an

increase in size must be discussed. It was not described in the ELCAP study (5) and the Framingham Heart Study defined an increase in size in the masses as a more than 20% increase in the longest diameter (6). In the current study by Yoon and colleagues (9), they defined an increase as an absolute increase in the long axis diameter of 2 mm or more. As some nodules/masses increased in size over time, the long-term management is still unclear.

According to previous reports, prognostic factors of thymomas were the Masaoka-Koga stage and increasing tumor size (11), and those of thymic malignancies were Masaoka or Masaoka-Koga stage and complete resection (12). Ten of 11 cases of TETs in the study by Yoon and colleagues were stage I and II, and all 11 cases were completely resected with no recurrence (median follow-up 67.0 months) (9). These results also suggest that the tumor size and an increase in size are important prognosis factors in TETs; however, the evidence supporting the benefit of early resection is limited and further study is required, as described in their discussion.

In summary, Yoon and colleagues (9) investigated the incidence of anterior mediastinal nodular lesions in a large population. However, the pathological diagnoses were not confirmed in all of the lesions, and it is still unclear what characteristics the nodules/masses must have to recommend resection or follow-up, or how long the patient should be followed. Moreover, nodules ≤5 mm have not been investigated, and it is unknown whether they need to be followed or not. Further investigations about the management of incidental anterior mediastinal nodular lesions over a long-period and in a large population will be necessary.

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Footnote

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