ACR Appropriateness Criteria® Imaging of Mediastinal Masses

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Abstract

Mediastinal masses can present with symptoms, signs, and syndromes or incidentally. Selecting the appropriate diagnostic imaging study for mediastinal mass evaluation requires awareness of the strengths and weaknesses of the various imaging modalities with regard to tissue characterization, soft tissue contrast, and surveillance. This publication expounds on the differences between chest radiography, CT, PET/CT, ultrasound, and MRI in terms of their ability to decipher and surveil mediastinal masses. Making the optimal imaging choice can yield diagnostic specificity, avert unnecessary biopsy and surgery, guide the interventionist when necessary, and serve as a means of surveillance for probably benign, but indeterminate mediastinal masses.

The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment.

Key Words: Appropriateness Criteria, Appropriate Use Criteria, AUC, CT, Mediastinal cyst, Mediastinal mass, MRI, Soft tissue contrast, Tissue characterization

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Variant 1. Clinically suspected mediastinal mass. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography chest	Usually Appropriate	☢
MRI chest without and with IV contrast	Usually Appropriate	O
MRI chest without IV contrast	Usually Appropriate	O
CT chest with IV contrast	Usually Appropriate	☢☢☢
CT chest without IV contrast	Usually Appropriate	☢☢☢
US chest	Usually Not Appropriate	O
Image-guided transthoracic needle biopsy	Usually Not Appropriate	Varies
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Variant 2. Indeterminate mediastinal mass on radiography. Next imaging study.

Procedure	Appropriateness Category	Relative Radiation Level
MRI chest without and with IV contrast	Usually Appropriate	O
MRI chest without IV contrast	Usually Appropriate	O
CT chest with IV contrast	Usually Appropriate	☢☢☢
CT chest without IV contrast	Usually Appropriate	☢☢☢
US chest	Usually Not Appropriate	O
Image-guided transthoracic needle biopsy	Usually Not Appropriate	Varies
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Variant 3. Indeterminate mediastinal mass on CT. Next imaging study.

Procedure	Appropriateness Category	Relative Radiation Level
MRI chest without and with IV contrast	Usually Appropriate	O
MRI chest without IV contrast	Usually Appropriate	O
Image-guided transthoracic needle biopsy	May Be Appropriate	Varies
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	☢☢☢☢
US chest	Usually Not Appropriate	O
Radiography chest	Usually Not Appropriate	☢

Variant 4. Indeterminate mediastinal mass on FDG-PET/CT. Next imaging study.

Procedure	Appropriateness Category	Relative Radiation Level
Image-guided transthoracic needle biopsy	Usually Appropriate	Varies
MRI chest without and with IV contrast	Usually Appropriate	O
MRI chest without IV contrast	Usually Appropriate	O
CT chest with IV contrast	May Be Appropriate	☢☢☢
US chest	Usually Not Appropriate	O
Radiography chest	Usually Not Appropriate	☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT chest without IV contrast	Usually Not Appropriate	☢☢☢

Variant 5. Indeterminate mediastinal mass on MRI. Next imaging study or surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
Image-guided transthoracic needle biopsy	Usually Appropriate	Varies
MRI chest without and with IV contrast	Usually Appropriate	O
MRI chest without IV contrast	May Be Appropriate	O
CT chest with IV contrast	May Be Appropriate	☢☢☢
CT chest without IV contrast	May Be Appropriate	☢☢☢
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	☢☢☢☢
US chest	Usually Not Appropriate	O
Radiography chest	Usually Not Appropriate	☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢

Table 1. Appropriateness category names and definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Table 2. Relative radiation level designations

RRL	Adult Effective Dose Estimate Range (mSv)	Pediatric Effective Dose Estimate Range (mSv)
O	0	0
☢	<0.1	<0.03
☢☢	0.1-1	0.03-0.3
☢☢☢	1-10	0.3-3
☢☢☢☢	10-30	3-10
☢☢☢☢☢	30-100	10-30

Note: Relative radiation level (RRL) assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "varies."

SUMMARY OF LITERATURE REVIEW

Introduction/Background

Although the true prevalence of mediastinal masses is not known, a 0.9% prevalence of anterior or prevascular mediastinal masses was found among the 2,571 chest CTs of the 51% female cohort of the Framingham Heart Study, with a mean age of 59 years [1]. A 0.73% prevalence of prevascular mediastinal nodules was found on the chest CTs of a 63% male cohort (n = 56,358 participants), with a mean age of 52 years, undergoing baseline low-dose chest CT for routine health surveillance [2]. A 4% prevalence of mediastinal masses was found on 589 CT pulmonary angiograms in a 63% female cohort with a mean age of 53 years [3]. On baseline lung cancer screening in the Early Lung Cancer Action Project, a 0.77% mediastinal mass prevalence was found in a cohort of 9,263 patients that was 51% female and had a median age of 65 years [4].

Although many mediastinal nodules or masses may present as incidental findings on chest radiographs and cross-sectional imaging, others present with symptoms, signs, and syndromes that include chest pain, cough, dyspnea, dysphagia, cardiac tamponade, diaphragmatic paralysis, central venous thrombosis, superior vena cava syndrome, B symptoms in the setting of lymphoma, myasthenia gravis, and other paraneoplastic syndromes. Other mediastinal masses present during staging and treatment of a known malignancy, including metastatic spread of disease to the mediastinum, rebound thymic hyperplasia, and acquired thymic cysts. Mediastinal lesions are also detected on lung cancer screening CTs [4] and during screening by cross-sectional imaging for patients with genetic mutations predisposing toward mediastinal masses, such as the succinate dehydrogenase subunits B and D mutations for paragangliomas [5,6] and the anti–*N*-methyl D-aspartate receptor antibody for teratomas [7]. Because mediastinal masses are so varied, not only in terms of benignity and malignancy but also in terms of their behavior, a general statement regarding their clinical course and treatment cannot be made.

Localization of a mediastinal mass to 1 of the 3 mediastinal compartments by chest radiography and cross-sectional imaging can narrow the differential diagnosis [8,9]. Cross-sectional imaging, by its very nature, can more definitively localize a lesion to a mediastinal compartment—hence the more recently prescribed use of cross-sectional imaging, rather than chest radiography, for definition of mediastinal compartments [10] and the use of new descriptive terms for the 3 mediastinal compartments—prevascular, visceral, and paravertebral—in lieu of anterior, middle, and posterior. A recently published international multi-institutional study confirmed the most common prevascular mediastinal lesions to be thymomas (28%), benign cysts (20%), and lymphomas (16%). Benign cysts were most common in the visceral compartment and neurogenic tumors were most common in the paravertebral compartment [11].

The classic imaging approach to mediastinal mass evaluation found on radiography has generally entailed a stepwise progression from chest radiography to CT [12-15] to diagnostic intervention when needed [16,17], with or without an intervening PET/CT. However, more recent recognition of the long-literature-supported ability of MRI to characterize tissue and add diagnostic specificity [18-23], prevent unnecessary biopsy and surgery [24-26], and modify and guide the approach to biopsy and surgery [27] has moved MRI into a valued position in terms of workup and triage of these lesions [28-33].

Special Imaging Considerations

For indeterminate hypervascular mediastinal masses on CT and MRI in typical locations for paraganglioma, Ga-68-

DOTATATE has the potential to make a specific diagnosis [34]; however, such additional testing may not be necessary if surgery is planned, regardless of histopathology. The role of Ga-68-DOTATATE PET/CT in the clinical management of thymic epithelial tumors (TETs) and the differentiation of neuroendocrine from non-neuroendocrine tumors needs further clarification, as somatostatin receptors are present in normal thymus and most TETs [35-37]. If ectopic thyroid tissue is a diagnostic consideration for an indeterminate prevascular or visceral mediastinal mass, Tc-99m pertechnetate or I-123 scintigraphy can be performed and can yield a specific diagnosis, although I-123 scintigraphy may be preferable because of its higher uptake in thyroid tissue and less background activity [38]. If extramedullary hematopoiesis is a diagnostic consideration for a paravertebral mass or multiple paravertebral masses, then Tc-99m sulfur colloid scintigraphy can be performed and can yield a specific diagnosis [39]. Imaging of parathyroid adenomas will be covered in a separate ACR Appropriateness Criteria® topic on "Parathyroid Adenoma" and therefore will not be discussed here.

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously in which each procedure provides unique clinical information to effectively manage the patient's care).

DISCUSSION OF PROCEDURES BY VARIANT

Variant 1: Clinically suspected mediastinal mass. Initial imaging

CT Chest. Cross-sectional imaging can more definitively localize a lesion to a mediastinal compartment than chest radiography. Further tissue characterization of mediastinal masses beyond chest radiography is achievable by CT, which can demonstrate and distinguish not only calcium and macroscopic fat but also water attenuation fluid, permitting noninvasive diagnosis of many mature teratomas [40]. Pre- and postcontrast conventional CT or dual-energy CT can show enhancing cellular components of lesions [41,42]; however, the soft tissue contrast of CT is sometimes insufficient. For example, benign hyperattenuating thymic cysts on CT can be misinterpreted as thymomas, leading to unnecessary thymectomy [24]. Not infrequently, a mediastinal lesion is indeterminate by CT and requires further workup.

CT is superior to chest radiography for detection of invasion of the mass across tissue planes, secondary to its higher contrast resolution. Invasion of adjacent large blood vessels and the chest wall is important to identify, as it is associated with a higher probability of incomplete surgical resection of primary malignant mediastinal masses [43]. In addition, it can direct surgery when still planned and, in other cases, direct toward other forms of clinical management, including neoadjuvant chemotherapy and radiation therapy. As a supplement to static assessment of tissue plane transgression, which can be difficult, dynamic CT [44] during free-breathing or cinematic cardiac gating, can be performed to assess movement of the mass relative to adjacent structures and confirm or exclude adherence of the mass to adjacent structures; however, dynamic MRI during free-breathing can accomplish the same task [45-48]. MRI remains superior to CT for detection of invasion of the mass across tissue planes, including the chest wall and diaphragm, and involvement of neurovascular structures, secondary to its higher soft tissue contrast [49-52].

FDG-PET/CT Skull Base to Mid-Thigh. Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT offers limited additional value beyond that of conventional CT in the initial assessment of mediastinal masses [53], with the exception of its use for primary mediastinal lymphoma staging and surveillance and detection of metastatic lymphadenopathy, the latter of which is not within the scope of this topic. With regard to prevascular mediastinal masses, a negative FDG-PET/CT has been shown to be helpful in excluding malignancy; however, a positive FDG-PET/CT has little value for discrimination between benign and malignant lesions [53]. The frequent FDG-PET/CT avidity of normal and hyperplastic thymus [54] is a confounder in FDG-PET/CT assessment of the prevascular mediastinum. Benign thymic cysts can also be FDG-PET/CT-avid [42]. Combined use of FDG-PET/CT and dynamic contrast-enhanced (DCE) MRI has been shown to be helpful to distinguish prevascular mediastinal solid tumors from one another [55]. Higher standardized uptake values (SUVs) on FDG-PET/CT are more frequently found in high-risk thymoma, thymic carcinoma, and lymphoma than in low-risk thymoma [55-57].

MRI Chest. MRI allows further tissue characterization of mediastinal masses beyond that of CT [21] and FDG-PET/CT because of its ability to detect not only serous fluid and macroscopic fat [58,59] but also hemorrhagic and

proteinaceous fluid [19,24], microscopic or intravoxel fat [22,60,61], cartilage [62,63], smooth muscle [64,65], and fibrous material [66-68], though not calcium. MRI can prove the cystic nature of an indeterminate, non–water attenuation thymic mass on CT, preventing unnecessary biopsy and thymectomy [20,21,24,69]. The ability of MRI to distinguish cystic from solid lesions definitively carries diagnostic importance in all compartments of the mediastinum. MRI can also show sites of restricted diffusion of water within lesions by employing diffusion-weighted imaging (DWI), further assisting in lesion characterization [70,71] DCE and postprocessed subtraction imaging can be used for further differentiation of lesions [55,72] and direction of biopsy toward areas of cellularity as opposed to hemorrhagic necrosis, the latter of which can be hyperattenuating and mimic solid tissue on CT. MRI is more useful than CT for evaluation of neurogenic tumors, because of its better depiction of neural and spinal involvement [73] and can be helpful in distinguishing schwannomas, neurofibromas, and ganglioneuromas [74-77], all of which may appear similar on CT. MRI can distinguish normal and hyperplastic thymus from thymic tumors and lymphoma, whether by chemical-shift MRI in adults [22,61] or by DWI with apparent diffusion coefficient (ADC) mapping [78,79], the latter with potential to make this distinction in all age groups. MRI can also help differentiate low-risk from high-risk thymomas, thymic carcinoma, and lymphoma by the DCE pattern of these lesions [72] and by DWI [71]. CT currently cannot achieve this degree of tissue characterization.

Cross-sectional imaging by MRI remains superior to CT for detection of invasion of the mass across tissue planes, including the chest wall and diaphragm, and involvement of neurovascular structures, secondary to its higher soft tissue contrast [48-52]. As a supplement to static assessment of tissue plane transgression, dynamic MRI [45-48] during free-breathing or cinematic cardiac gating can be performed to assess movement of the mass relative to adjacent structures, confirm or exclude adherence of the mass to adjacent structures, and observe diaphragmatic motion in real time [80-84]; paradoxical motion or lack of motion can indicate phrenic nerve involvement by the mediastinal mass, without the need to perform a subsequent fluoroscopic sniff test.

Radiography Chest. When there is a clinically suspected mediastinal mass, it is reasonable to perform a chest radiograph as an initial imaging step. Chest radiography can help localize a mass to a specific mediastinal compartment and thereby narrow the differential diagnosis [85-88]. It can also show any associated pleural, lung, and bone findings to some extent. Chest radiography offers limited assistance regarding tissue characterization of mediastinal masses, with the exception of its occasional demonstration of calcium within a lesion.

US Chest. There is little relevant literature to support the use of ultrasound (US) in the initial evaluation of a clinically suspected mediastinal mass. Because of the limited transthoracic sonographic window, US would not be useful to screen for a clinically suspected mediastinal mass. Transthoracic US can be used to evaluate mediastinal masses, when accessible to the sonographic window, delineating their size, location, cystic versus solid nature, relationship to important vascular structures, and vascularity, with some diagnostic potential [89]. Endoscopic US can similarly evaluate mediastinal masses when encompassed in the sonographic window [90]. The tissue characterization capability of US is inferior to MRI but not to CT.

Image-Guided Transthoracic Needle Biopsy. Image-guided transthoracic needle biopsy is not a form of initial imaging.

Variant 2: Indeterminate mediastinal mass on radiography. Next imaging study

CT Chest. Cross-sectional imaging, by its very nature, can more definitively localize a lesion to a mediastinal compartment than chest radiography. Further tissue characterization of mediastinal masses beyond chest radiography is achievable by CT, which can demonstrate and distinguish not only calcium and macroscopic fat but also water attenuation fluid, thus permitting noninvasive diagnosis of many mature teratomas [40]. Pre- and postcontrast conventional CT or dual-energy CT can show enhancing, cellular components of lesions [41,42]; however, the soft tissue contrast of CT is sometimes insufficient. For example, benign hyperattenuating thymic cysts on CT can be misinterpreted as thymomas, leading to unnecessary thymectomy [24]. Not infrequently, a mediastinal lesion is indeterminate by CT and requires further workup.

CT is superior to chest radiography for detection of invasion of the mass across tissue planes, secondary to its higher contrast resolution. Invasion of adjacent large blood vessels and the chest wall is important to identify, as it is associated with a higher probability of incomplete surgical resection of primary malignant mediastinal masses [43]. In addition, it can direct surgery when still planned, and in other cases, direct toward other forms of clinical management, including neoadjuvant chemotherapy and radiation therapy. As a supplement to static assessment of tissue plane transgression, which can be difficult, dynamic CT [44] during free-breathing or cinematic cardiac gating

can be performed to assess movement of the mass relative to adjacent structures and to confirm or exclude adherence of the mass to adjacent structures; however, dynamic MRI during free-breathing can accomplish the same task [45-48]. MRI remains superior to CT for detection of invasion of the mass across tissue planes, including the chest wall and diaphragm, and involvement of neurovascular structures, secondary to its higher soft tissue contrast [49-52].

FDG-PET/CT Skull Base to Mid-Thigh. FDG-PET/CT offers limited additional value beyond that of conventional CT in the assessment of mediastinal masses [53], with the exception of its use for primary mediastinal lymphoma staging and surveillance and detection of metastatic lymphadenopathy, the latter of which is not within the scope of this topic. FDG-PET/CT has become the standard for staging and assessment of treatment response for lymphomas that are FDG-PET-avid at baseline or at the time of recurrence [91-97]. A caveat is that although a negative surveillance FDG-PET/CT is reassuring of a good outcome, a positive FDG-PET/CT can be misleading, as it does not always implicate residual or recurrent lymphoma [96,98]. CT and MRI can be used for surveillance of lymphadenopathy when the metabolic activity of the lymphadenopathy is not of interest and when allowed within a clinical protocol. With regard to prevascular mediastinal masses, a negative FDG-PET/CT has been shown to be helpful in excluding malignancy; however, a positive FDG-PET/CT has little value for discrimination between benign and malignant lesions [53]. The frequent FDG-PET/CT avidity of normal and hyperplastic thymus [54] is a confounder in FDG-PET/CT assessment of the prevascular mediastinum. Benign thymic cysts can also be FDG-PET/CT-avid [42]. Combined use of FDG-PET/CT and DCE MRI has been shown to be helpful to distinguish prevascular mediastinal solid tumors from one another [55]. Higher SUVs on FDG-PET/CT are more frequently found in high-risk thymoma, thymic carcinoma, and lymphoma than in low-risk thymoma [55-57]. FDG-PET/CT appears to be more sensitive than CT alone for detection of mediastinal recurrence of thymoma [99].

MRI Chest. MRI allows further tissue characterization of mediastinal masses beyond that of CT [21] and FDG-PET/CT because of its ability to detect not only serous fluid and macroscopic fat [58,59] but also hemorrhagic and proteinaceous fluid [19,24], microscopic or intravoxel fat [22,60,61], cartilage [62,63], smooth muscle [64,65], and fibrous material [66-68], though not calcium. MRI can prove the cystic nature of an indeterminate, non–water attenuation thymic mass on CT, preventing unnecessary biopsy and thymectomy [20,21,24,69]. The ability of MRI to distinguish cystic from solid lesions definitively carries diagnostic importance in all compartments of the mediastinum. MRI can also show sites of restricted diffusion of water within lesions by employing DWI, further assisting in lesion characterization [70,71] and can employ DCE and postprocessed subtraction imaging for further differentiation of lesions [55,72] and for direction of biopsy toward areas of cellularity, as opposed to hemorrhagic necrosis, the latter of which can be hyperattenuating and mimic solid tissue on CT. MRI is more useful than CT for evaluation of neurogenic tumors, because of its better depiction of neural and spinal involvement [73], and it can be helpful in distinguishing schwannomas, neurofibromas, and ganglioneuromas [74-77], all of which may appear similar on CT. MRI can distinguish normal and hyperplastic thymus from thymic tumors and lymphoma, whether by chemical-shift MRI in adults [22,61] or by DWI with ADC mapping [78,79], the latter with potential to make this distinction in all age groups. MRI can also help differentiate low-risk from high-risk thymomas, thymic carcinoma, and lymphoma by the DCE pattern of these lesions [72] and by DWI [71]. CT currently cannot achieve this degree of tissue characterization. MRI has been shown to be slightly superior to CT for surveillance of treated TETs, although, if there is insurmountable susceptibility artifact from sternotomy wires using fast spin-echo and other MRI techniques, alternating MRI and CT follow-up can be performed [100].

Cross-sectional imaging by MRI remains superior to CT for detection of invasion of the mass across tissue planes, including the chest wall and diaphragm, and involvement of neurovascular structures, secondary to its higher soft tissue contrast [48-52]. As a supplement to static assessment of tissue plane transgression, dynamic MRI [45-48] during free-breathing or cinematic cardiac gating can be performed to assess movement of the mass relative to adjacent structures, confirm or exclude adherence of the mass to adjacent structures, and observe diaphragmatic motion in real time [80-84]; paradoxical motion or lack of motion can indicate phrenic nerve involvement by the mediastinal mass, without the need to perform a subsequent fluoroscopic sniff test.

US Chest. Unless a mediastinal mass found on chest radiography is deemed fully accessible by transthoracic US, there is little relevant literature to support its use as the next step. Transthoracic US can be used to evaluate mediastinal masses, when accessible to the sonographic window, delineating their size, location, cystic versus solid nature, relationship to important vascular structures, and vascularity, with some diagnostic potential [89]. Endoscopic US can similarly evaluate mediastinal masses when encompassed in

the sonographic window [90]. The tissue characterization capability of US is inferior to MRI but not to CT.

Image-Guided Transthoracic Needle Biopsy. Image-guided transthoracic needle biopsy would seldom be performed without a preceding cross-sectional imaging study.

Variant 3: Indeterminate mediastinal mass on CT. Next imaging study

FDG-PET/CT Skull Base to Mid-Thigh. FDG-PET/CT offers limited additional value beyond that of conventional CT in the assessment of mediastinal masses [53], with the exception of its use for primary mediastinal lymphoma staging and surveillance and detection of metastatic lymphadenopathy, the latter of which is not within the scope of this topic. FDG-PET/CT has become the standard for staging and assessment of treatment response for lymphomas that are FDG-PET-avid at baseline or at the time of recurrence [91-97]. A caveat is that although a negative surveillance FDG-PET/CT is reassuring of a good outcome, a positive FDG-PET/CT can be misleading, as it does not always implicate residual or recurrent lymphoma [96,98]. CT and MRI can be used for surveillance of lymphadenopathy, when the metabolic activity of the lymphadenopathy is not of interest and when allowed within a clinical protocol. With regard to prevascular mediastinal masses, a negative FDG-PET/CT has been shown to be helpful in excluding malignancy; however, a positive FDG-PET/CT has little value for discrimination between benign and malignant lesions [53]. The frequent FDG-PET/CT avidity of normal and hyperplastic thymus [54] is a confounder in FDG-PET/CT assessment of the prevascular mediastinum. Benign thymic cysts can also be FDG-PET/CT-avid [42]. Combined use of FDG-PET/CT and DCE MRI has been shown to be helpful to distinguish prevascular mediastinal solid tumors from one another [55]. Higher SUVs on FDG-PET/CT are more frequently found in high-risk thymoma, thymic carcinoma, and lymphoma than in low-risk thymoma [55-57]. FDG-PET/CT appears to be more sensitive than CT alone for detection of mediastinal recurrence of thymoma [99].

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US Chest. There is little relevant literature to support US of an indeterminate mediastinal mass on CT. Transthoracic US can be used to evaluate mediastinal masses when accessible to the sonographic window, delineating their size, location, cystic versus solid nature, relationship to important vascular structures, and vascularity, with some diagnostic potential [89]. Endoscopic US can similarly evaluate mediastinal masses when encompassed in the sonographic

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Image-Guided Transthoracic Needle Biopsy. CT-guided percutaneous needle and core biopsy of accessible mediastinal masses has been shown to be safe and to have a good diagnostic yield, with core biopsy more effective than fine-needle aspiration. Biopsy was more frequently diagnostic for TETs than for lymphoma [101-104]. A retrospective study of 293 consecutive CT-guided mediastinal biopsies performed in 285 patients showed an overall diagnostic yield of 87% for mediastinal masses with a mean size of 5.3 cm and 57% for residual masses at the site of treated lymphoma [101]. Another retrospective study of 52 patients reported a 77% diagnostic yield for needle biopsy of mediastinal masses with a mean size of 6.9 cm [102]. When the distinction of TETs from lymphoma cannot be definitively made by imaging, image-guided biopsy has a role. PET/CT guidance for biopsy reportedly yields no diagnostic advantage [104]. When the lesion is visible within the sonographic window, transthoracic US-guided biopsy of mediastinal masses is also feasible, with color Doppler and contrast-enhanced sonographic techniques providing additional value [105-108] and with core biopsy more effective than fine-needle aspiration. Endoscopic biopsy of mediastinal masses is also feasible and effective, although not in the purview of this topic [109]. DWI MR may be helpful in directing CT-guided biopsy toward sites of higher cellularity and diagnostic yield [110], as may DCE MRI with postprocessed subtraction. MR-guided percutaneous needle biopsy has also been shown to be safe and diagnostically accurate [111].

Radiography Chest. After cross-sectional imaging has been performed for mediastinal mass evaluation, there is seldom a role for chest radiography.

Variant 4: Indeterminate mediastinal mass on FDG-PET/CT. Next imaging study

CT Chest. After FDG-PET/CT has been performed for mediastinal mass evaluation, there is seldom a role for chest CT.

MRI Chest. MRI allows further tissue characterization of mediastinal masses beyond that of CT [21] and FDG-PET/CT because of its ability to detect not only serous fluid and macroscopic fat [58,59] but also hemorrhagic and proteinaceous fluid [19,24], microscopic or intravoxel fat [22,60,61], cartilage [62,63], smooth muscle [64,65], and fibrous material [66-68], though not calcium. MRI can prove the cystic nature of an indeterminate, non–water attenuation thymic mass on CT, preventing unnecessary biopsy and thymectomy [20,21,24,69]. The ability of MRI to distinguish cystic from solid lesions definitively carries diagnostic importance in all compartments of the mediastinum. MRI can also show sites of restricted diffusion of water within lesions by employing DWI, further assisting in lesion characterization [70,71], and can employ DCE and postprocessed subtraction imaging for further differentiation of lesions [55,72] and for direction of biopsy toward areas of cellularity, as opposed to hemorrhagic necrosis, the latter of which can be hyperattenuating and mimic solid tissue on CT. MRI is more useful than CT for evaluation of neurogenic tumors, because of its better depiction of neural and spinal involvement [73], and it can be helpful in distinguishing schwannomas, neurofibromas, and ganglioneuromas [74-77], all of which may appear similar on CT. MRI can distinguish normal and hyperplastic thymus from thymic tumors and lymphoma, whether by chemical-shift MRI in adults [22,61] or by DWI with ADC mapping [78,79], the latter with potential to make this distinction in all age groups. MRI can also help differentiate low-risk from high-risk thymomas, thymic carcinoma, and lymphoma by the DCE pattern of these lesions [72] and by DWI [71]. CT currently cannot achieve this degree of tissue characterization. MRI has been shown to be slightly superior to CT for surveillance of treated TETs, although if there is insurmountable susceptibility artifact from sternotomy wires using fast spin-echo and other MRI techniques, alternating MRI and CT follow-up can be performed [100].

Cross-sectional imaging by MRI remains superior to CT for detection of invasion of the mass across tissue planes, including the chest wall and diaphragm, and involvement of neurovascular structures, secondary to its higher soft tissue contrast [48-52]. As a supplement to static assessment of tissue plane transgression, dynamic MRI [45-48] during free-breathing or cinematic cardiac gating can be performed to assess movement of the mass relative to adjacent structures, confirm or exclude adherence of the mass to adjacent structures, and observe diaphragmatic motion in real time [80-84]; paradoxical motion or lack of motion can indicate phrenic nerve involvement by the mediastinal mass, without the need to perform a subsequent fluoroscopic sniff test.

US Chest. There is little relevant literature to support US of an indeterminate mediastinal mass on FDG-PET/CT. Transthoracic US can be used to evaluate mediastinal masses when accessible to the sonographic window, delineating their size, location, cystic versus solid nature, relationship to important vascular structures, and vascularity, with some diagnostic potential [89]. Endoscopic US can

similarly evaluate mediastinal masses when encompassed in the sonographic window [90]. The tissue characterization capability of US is inferior to MRI but not to CT.

Image-Guided Transthoracic Needle Biopsy. CT-guided percutaneous needle and core biopsy of accessible mediastinal masses has been shown to be safe and to have a good diagnostic yield, with core biopsy more effective than fine-needle aspiration. Biopsy was more frequently diagnostic for TETs than for lymphoma [101-104]. A retrospective study of 293 consecutive CT-guided mediastinal biopsies performed in 285 patients showed an overall diagnostic yield of 87% for mediastinal masses with a mean size of 5.3 cm and 57% for residual masses at the site of treated lymphoma [101]. Another retrospective study of 52 patients reported a 77% diagnostic yield for needle biopsy of mediastinal masses with a mean size of 6.9 cm [102]. When the distinction of TETs from lymphoma cannot be definitively made by imaging, image-guided biopsy has a role. PET/CT guidance for biopsy reportedly yields no diagnostic advantage [104]. When the lesion is visible within the sonographic window, transthoracic US-guided biopsy of mediastinal masses is also feasible, with color Doppler and contrast-enhanced sonographic techniques providing additional value [105-108], and with core biopsy more effective than fine-needle aspiration. Endoscopic biopsy of mediastinal masses is also feasible and effective, although not in the purview of this topic [109]. DWI MR may be helpful in directing CT-guided biopsy toward sites of higher cellularity and diagnostic yield [110], as may DCE MRI with postprocessed subtraction. MR-guided percutaneous needle biopsy has also been shown to be safe and diagnostically accurate [111].

Radiography Chest. After cross-sectional imaging has been performed for mediastinal mass evaluation, there is seldom a role for chest radiography.

Variant 5: Indeterminate mediastinal mass on MRI. Next imaging study or surveillance

CT Chest. Unless there is concern for missed calcification within a mediastinal mass and any diagnostic utility such a finding may have, CT would be unlikely to add additional diagnostic information regarding a mediastinal mass beyond that offered by MRI. CT can be used as a means of follow-up of indeterminate mediastinal masses, readily showing any change in size, morphology, or attenuation of the lesion. However, surveillance by CT would be less likely to provide the level of diagnostic certainty that MR could provide at follow-up on account of MR's greater sensitivity for detection of increased lesion complexity and its greater capacity to characterize tissue. Surveillance could be performed at a 3-, 6-, or 12-month interval over 2 or more years, depending upon the level of clinical concern.

FDG-PET/CT Skull Base to Mid-Thigh. Unless the degree of metabolic activity of a mediastinal mass is sought and deemed capable of changing clinical management, FDG-PET/CT would be unlikely to add diagnostic information regarding a mediastinal mass beyond that offered by MRI. FDG-PET/CT offers limited additional value beyond that of conventional CT and MRI in the assessment of mediastinal masses [53], with the exception of its use for primary mediastinal lymphoma staging and surveillance and detection of metastatic lymphadenopathy, the latter of which is not within the scope of this topic. FDG-PET/CT has become the standard for staging and assessment of treatment response for lymphomas that are FDG-PET-avid at baseline or at the time of recurrence [91-97]. A caveat is that although a negative surveillance FDG-PET/CT is reassuring of a good outcome, a positive FDG-PET/CT can be misleading, as it does not always implicate residual or recurrent lymphoma [96,98]. With regard to prevascular mediastinal masses, a negative FDG-PET/CT has been shown to be helpful in excluding malignancy; however, a positive FDG-PET/CT has little value for discrimination between benign and malignant lesions [53]. The frequent FDG-PET/CT avidity of normal and hyperplastic thymus [54] is a confounder in FDG-PET/CT assessment of the prevascular mediastinum. Benign thymic cysts can also be FDG-PET/CT-avid [42]. Combined use of FDG-PET/CT and DCE MRI has been shown to be helpful to distinguish prevascular mediastinal solid tumors from one another [55]. Higher SUVs on FDG-PET/CT are more frequently found in high-risk thymoma, thymic carcinoma, and lymphoma than in low-risk thymoma [55-57]. FDG-PET/CT appears to be more sensitive than CT alone for detection of mediastinal recurrence of thymoma [99].

MRI Chest. Sometimes a mediastinal mass is found and incompletely evaluated on chest MR angiography or a neck, breast, abdominal, spine, or chest wall MRI and more dedicated chest MR evaluation is needed. When a mediastinal mass is indeterminate on MRI after more comprehensive evaluation, a short-term follow-up chest MRI can be performed, rather than proceeding to biopsy or resection, at a 3-, 6-, or 12-month interval over 2 or more years, depending upon the level of clinical concern. MRI can not only provide information about any interval change in size or morphology, which CT can accomplish, but can also provide additional detail regarding lesion complexity and tissue characterization beyond that of CT [21] and FDG-PET/CT. This added value is due to its ability to detect not only serous fluid and macroscopic fat [58,59] but also hemorrhagic and proteinaceous fluid [19,24], microscopic or intravoxel fat [22,60,61], cartilage [62,63], smooth

muscle [64,65], and fibrous material [66-68], though not calcium. MRI can prove the cystic nature of an indeterminate, non–water attenuation thymic mass on CT, preventing unnecessary biopsy and thymectomy [20,21,24,69]. The ability of MRI to distinguish cystic from solid lesions definitively carries diagnostic importance in all compartments of the mediastinum. MRI can also show sites of restricted diffusion of water within lesions by employing DWI, further assisting in lesion characterization [70,71], and can employ DCE and postprocessed subtraction imaging for further differentiation of lesions [55,72] and for direction of biopsy toward areas of cellularity, as opposed to hemorrhagic necrosis, the latter of which can be hyperattenuating and mimic solid tissue on CT. MRI is more useful than CT for evaluation of neurogenic tumors, because of its better depiction of neural and spinal involvement [73], and can be helpful in distinguishing schwannomas, neurofibromas, and ganglioneuromas [74-77], all of which may appear similar on CT. MRI can distinguish normal and hyperplastic thymus from thymic tumors and lymphoma, whether by chemical-shift MRI in adults [22,61] or by DWI with ADC mapping [78,79], the latter with potential to make this distinction in all age groups. MRI can also help differentiate low-risk from high-risk thymomas, thymic carcinoma, and lymphoma by the DCE pattern of these lesions [72] and by DWI [71]. CT currently cannot achieve this degree of tissue characterization. MRI has been shown to be slightly superior to CT for surveillance of treated TETs, although if there is insurmountable susceptibility artifact from sternotomy wires despite use of fast spin-echo and other MRI techniques, alternating MRI and CT follow-up can be performed [100].

Cross-sectional imaging by MRI remains superior to CT for detection of invasion of the mass across tissue planes, including the chest wall and diaphragm, and involvement of neurovascular structures, secondary to its higher soft tissue contrast [48-52]. As a supplement to static assessment of tissue plane transgression, dynamic MRI [45-48] during free-breathing or cinematic cardiac gating can be performed to assess movement of the mass relative to adjacent structures, to confirm or exclude adherence of the mass to adjacent structures, and to observe diaphragmatic motion in real time [80-84]; paradoxical motion or lack of motion can indicate phrenic nerve involvement by the mediastinal mass, without the need to perform a subsequent fluoroscopic sniff test.

US Chest. Transthoracic US is unlikely to offer additional information regarding mediastinal mass characterization beyond that of MRI.

Image-Guided Transthoracic Needle Biopsy. CT-guided percutaneous needle and core biopsy of accessible mediastinal masses has been shown to be safe and to have a good diagnostic yield, with core biopsy more effective than fine-needle aspiration. Biopsy was more frequently diagnostic for TETs than for lymphoma [101-104]. A retrospective study of 293 consecutive CT-guided mediastinal biopsies performed in 285 patients showed an overall diagnostic yield of 87% for mediastinal masses with a mean size of 5.3 cm and 57% for residual masses at the site of treated lymphoma [101]. Another retrospective study of 52 patients reported a 77% diagnostic yield for needle biopsy of mediastinal masses with a mean size of 6.9 cm [102]. When the distinction of TETs from lymphoma cannot be definitively made by imaging, image-guided biopsy has a role. PET/CT guidance for biopsy reportedly yields no diagnostic advantage [104]. When the lesion is visible within the sonographic window, transthoracic US-guided biopsy of mediastinal masses is also feasible, with color Doppler and contrast-enhanced sonographic techniques providing additional value [105-108], and with core biopsy more effective than fine-needle aspiration. Endoscopic biopsy of mediastinal masses is also feasible and effective, although not in the purview of this topic [109]. DWI MR may be helpful in directing CT-guided biopsy toward sites of higher cellularity and diagnostic yield [110], as may DCE MRI with postprocessed subtraction. MR-guided percutaneous needle biopsy has also been shown to be safe and diagnostically accurate [111].

Radiography Chest. After cross-sectional imaging has been performed for mediastinal mass evaluation, there is a seldom a role for chest radiography.

SUMMARY OF RECOMMENDATIONS

- **Variant 1:** Radiography chest or MRI chest without and with intravenous (IV) contrast or MRI chest without IV contrast or CT chest without IV contrast or CT chest with IV contrast or CT chest without IV contrast is usually appropriate for the initial imaging of patients with clinically suspected mediastinal mass. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 2:** MRI chest without and with IV contrast or MRI chest without IV contrast or CT chest with IV contrast or CT chest without IV contrast is usually appropriate for the next imaging study of patients with indeterminate mediastinal mass on radiography. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).

- **Variant 3:** MRI chest without and with IV contrast or MRI chest without IV contrast is usually appropriate for the next imaging study of patients with indeterminate mediastinal mass on CT. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 4:** Image-guided transthoracic needle biopsy or MRI chest without and with IV contrast or MRI chest without IV contrast is usually appropriate for the next imaging study of patients with indeterminate mediastinal mass on FDG-PET/CT. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 5:** Image-guided transthoracic needle biopsy or MRI chest without and with IV contrast is usually appropriate for the next imaging study or surveillance of patients with indeterminate mediastinal mass on MRI. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).

SUPPORTING DOCUMENTS

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

RELATIVE RADIATION LEVEL INFORMATION

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table 2). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [112].

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