**Clinical Condition:** Clinically Suspected Pulmonary Arteriovenous Malformation (PAVM)

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
<th>RRL*</th>
</tr>
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<tbody>
<tr>
<td>US echocardiography transthoracic bubble study</td>
<td>8</td>
<td>This procedure is often used following positive TTE.</td>
<td>O</td>
</tr>
<tr>
<td>CTA chest with IV contrast</td>
<td>8</td>
<td></td>
<td>☢☢☢</td>
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<tr>
<td>X-ray chest</td>
<td>7</td>
<td>This procedure is complementary to other examinations, such as TTE.</td>
<td>☩</td>
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<tr>
<td>US echocardiography transesophageal bubble study</td>
<td>6</td>
<td>This procedure is the reference standard for detecting right-to-left shunts but is more invasive than TTE.</td>
<td>☩</td>
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<tr>
<td>MRA chest without and with IV contrast</td>
<td>6</td>
<td></td>
<td>O</td>
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<tr>
<td>CT chest without IV contrast</td>
<td>6</td>
<td></td>
<td>☢☢</td>
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<tr>
<td>Arteriography pulmonary</td>
<td>5</td>
<td>Although this procedure is appropriate for preinterventional planning, it is usually not appropriate as an initial test.</td>
<td>☢☢☢</td>
</tr>
<tr>
<td>US transcranial bubble study</td>
<td>5</td>
<td>This procedure is an alternative to TTE, although it is less widely available.</td>
<td>☩</td>
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<tr>
<td>Pertechnetate albumin pulmonary scan</td>
<td>4</td>
<td></td>
<td>☢☢☢</td>
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<tr>
<td>MRA chest without IV contrast</td>
<td>3</td>
<td></td>
<td>O</td>
</tr>
</tbody>
</table>

**Rating Scale:** 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level*
Expert Panel on Vascular Imaging: Michael Hanley, MD; Osmanuddin Ahmed, MD; Ankur Chandra, MD; Kenneth L. Gage, MD, PhD; Marie D. Gerhard-Herman, MD; Michael Ginsburg, MD; Heather L. Gornik, MD; Pamela T. Johnson, MD; Isabel B. Oliva, MD; Thomas Ptak, MD, PhD; Michael L. Steigner, MD; Richard Strax, MD; Frank J. Rybicki, MD, PhD; Karin E. Dill, MD.

Summary of Literature Review

Introduction/Background

Pulmonary arteriovenous malformations (PAVMs) are vascular structures that most commonly result from abnormal communication between pulmonary arteries and pulmonary veins. The majority of PAVMs are congenital in nature due to a developmental defect in the capillary bed resulting in a right-to-left intrapulmonary shunt. PAVMs are more often solitary and simple, although multiple and/or complex forms are described [1]. Although PAVMs <2 cm are usually asymptomatic, larger AVMs can cause clinical symptoms [1]. Although uncommon, PAVMs are often considered in the differential diagnosis of common disease states including hypoxemia, hemoptysis, brain abscesses, and paradoxical stroke, as well as in the differential for pulmonary nodules.

Approximately 90% of PAVMs occur in patients with hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome [1]. HHT is an autosomal dominant disease with variable expression and an estimated prevalence of 1 in 5000 [2]. HHT commonly presents with epistaxis or visible mucocutaneous telangiectasia and is often complicated by PAVMs as well as vascular malformations of the brain, gastrointestinal tract, and liver. The incidence of PAVMs in patients with HHT is 30%–50% [1]. HHT is classically a clinical diagnosis, and although genetic testing is available, it remains complex due to multiple mutations that are family specific.

In addition to the congenital PAVMs common to HHT, PAVMs can also be acquired through trauma or infection [1], associated with hepatopulmonary syndrome in the setting of chronic liver disease [3], or after surgical repair of congenital heart disease (bidirectional cavopulmonary shunt) [4].

PAVMs do not have malignant potential, but they can enlarge with time and require follow-up [1]. The treatment of PAVMs has traditionally been recommended when the feeding vessel is >3 mm, regardless of the clinical presentation, due primarily to potential neurological complications [5]. However, more recent reports of PAVMs with feeding vessels <3 mm causing symptomatic paradoxical emboli has resulted in many centers treating PAVMs smaller than the previously established cutoff [6]. Technical factors can limit the treatment of PAVMs with feeding vessels <1.5 mm [6]. After successful embolization of PAVMs, echocardiography often remains positive, so patients often begin lifelong follow-up in 3- to 5-year intervals with computed tomography (CT) or magnetic resonance angiography (MRA) [1,6,7].

Echocardiography

Although transesophageal echocardiography bubble studies are considered the reference standard to screen for right-to-left shunt, transthoracic echocardiography (TTE) bubble studies are more commonly used given noninvasiveness and low cost [8,9].

A TTE bubble study uses agitated saline as a contrast agent and is considered positive for a right-to-left shunt when microbubbles are visualized in the left atrium after 3–8 cardiac cycles. A grading system (0–3) has been...
developed that correlates with the presence of PAVMs on CT and also with neurological complications [10, 11]. However, this modality does not provide anatomical information such as size and location of PAVMs.

Cottin et al [5] reviewed the diagnostic accuracy of screening for PAVMs with chest radiographs, alveolar-arterial \( \text{PO}_2 \) gradient, TTE bubble studies, and radionuclide pulmonary scintigraphy in 105 patients with HHT. This retrospective review used CT and/or pulmonary angiography (PA) as the reference standard. TTE bubble study was the most sensitive (93%) for the diagnosis of PAVMs, followed by radionuclide scintigraphy (71%), chest radiograph (70%), and alveolar-arterial \( \text{PO}_2 \) gradient (62%). Combining TTE bubble studies and chest radiographs led to 100% sensitivity and specificity.

Van Gent et al [12] prospectively evaluated patients for PAVMs who were referred for HHT screening. Patients (n = 299) underwent a TTE bubble study, noncontrast high resolution CT (HRCT), arterial blood gas analysis, and chest radiography. HRCT was used as the reference standard. Sensitivity of the TTE bubble study was 97%, specificity was 77%, and the negative predictive value was 99%.

The International Guidelines for the Diagnosis and Management of HHT recommends initial screening with a TTE bubble study, followed by thin-section (1–2 mm) CT for positive cases [2]. TTE bubble studies can remain positive in 80% of patients after successful treatment of PAVM [13].

**Transcranial Ultrasound**

Manawadu et al [14] evaluated ultrasound (US) transcranial bubble studies in 12 patients with HHT in comparison with TTE bubble studies using CT or CT angiography (CTA) as the reference standard. Positive studies demonstrated microbubbles in the middle cerebral artery with a combination of M-mode and spectroscopy after 3–7 cardiac cycles after the injection of agitated saline. Both transcranial US and TTE had high sensitivity (100%) and low specificity (38% and 25%, respectively). Although transcranial US could be used as an alternative to TTE, it is less widely available.

**Chest Radiograph**

Chest radiographs are well established as an initial imaging modality for patients presenting with hypoxemia or hemoptysis [15], as well as having the ability to suggest alternative diagnoses in patients suspected of having PAVMs. However, chest radiographs alone suffer from low sensitivity to adequately screen patients with suspected PAVMs and may not detect clinically treatable PAVMs. Cottin et al [5] reported a sensitivity of 70% and specificity of 98% in 105 patients with HHT. The use of chest radiographs in conjunction with TTE bubble studies can provide 100% sensitivity and specificity in the same study group. Van Gent et al [12] reported a sensitivity of 28% and specificity of 100% in 296 patients presenting for HHT screening.

**Computed Tomography and Computed Tomography Angiography**

Unlike imaging modalities designed to detect right-to-left shunts, CT provides detailed anatomical information for pretreatment planning. Remy et al [16] demonstrated the utility of thin-section noncontrast CT with 3-D reconstructions in detecting PAVMs prior to PA with a 95% detection rate. The International Guidelines for the Diagnosis and Management of HHT [2] recommends thin-section (1–2 mm) noncontrast CT to follow a positive screening TTE bubble study. After treatment of PAVMs, Trerotola and Pyeritz [6] recommended patients begin lifelong follow-up with CTA starting at 6 months and continuing at 3- to 5-year intervals. The added benefit of performing a contrast CT pulmonary angiogram must be weighed against the risk of introducing air and paradoxical embolus [6].

Nawaz et al [17] compared CTA and PA in the detection of PAVM in 18 patients with HHT. More PAVMs were detected with CTA than with PA. During the analysis of 42 PAVMs, CTA was reported to have a higher mean sensitivity (83%) compared to PA (68%) but with slightly lower specificity (93% versus 100%, respectively). The use of planar reconstruction, 3-D, and maximum-intensity projections can assist detection [1, 17].

**Magnetic Resonance Angiography**

Like CT, contrast-enhanced MRA (CE-MRA) provides anatomical information for pretreatment planning. The avoidance of ionizing radiation is particularly important in the HHT population, who are screened often and potentially starting at a young age.

Schneider et al [7] evaluated CE-MRA for the detection of PAVMs in 203 patients with HHT. Detected PAVMs ≥5 mm subsequently underwent PA for possible embolization. CE-MRA detected more PAVMs than PA (119 versus 92), but not all patients underwent PA. Boussel et al [18] demonstrated the value of time-resolved MRA to
assess patency of known PAVMs in patients with HHT. There are inherent limitations of MRA in detecting PAVMs <5 mm, which may have clinical consequences because many centers are treating PAVMs below the established threshold of a 3-mm feeding vessel [6]. Shimohira et al [19] reported on their use of time-resolved MRA in follow-up of treated PAVMs. They demonstrated 49% reperfusion rate at 24 months for primary embolization and 100% for repeat embolization, confirming the need for continued surveillance.

**Pulmonary Scintigraphy**

Right-to-left shunts can be detected by intravenous injection of Tc-99m pertechnetate-labeled albumin. The injected particles measure ≥20 µm and are normally trapped in the capillary bed of the lung [1]. Abnormal activity in the kidney or brain can be seen in the presence of PAVMs, and calculation of a shunt fraction can be performed. Cottin et al [5] reported pulmonary scintigraphy has a sensitivity of 71% in the screening of patients with HHT for PAVMs, only slightly better than chest radiographs. Whyte et al [20] demonstrated agreement between pulmonary scintigraphy and shunt fractions calculated during 100% oxygen arterial blood gas analysis. Thompson et al [21] reported sensitivity and specificity of 87% and 61% for pulmonary scintigraphy in detection of PAVM in patients with HHT. Pulmonary scintigraphy does not provide anatomical information for pretreatment planning or determine who may be eligible for treatment. Similar to TTE bubble studies, pulmonary scintigraphy can remain positive after treatment of PAVMs due to occult lesions or PAVMs that are too small to treat.

**Pulmonary Angiography**

PA has traditionally been the reference standard for detection of PAVMs, as described in the studies by Schneider and Nawaz. Schneider et al [7] demonstrated significantly fewer PAVMs detected on PA when compared with CE-MRA. Nawaz et al [17] demonstrated PA had improved specificity (100% versus 78%) at the cost of sensitivity (70% versus 83%) when compared to CT. Diagnostic PA does remain a critical component of the treatment of PAVMs when performed with concurrent transcatheter embolization.

**Summary of Recommendations**

- A chest radiograph is usually appropriate in that it is complementary to TTE and may suggest an alternative diagnosis.
- The International Guidelines for the Diagnosis and Management of HHT recommends initial screening with a TTE bubble study, followed by thin-section (1–2 mm) CT for positive cases. The added benefit of performing a contrast CT pulmonary angiogram must be weighed against the risk of introducing air and paradoxical embolus.
- Noninvasive imaging examinations including TTE bubble studies and radionuclide perfusion are designed to detect the presence of right-to-left shunts. These, however, do not provide anatomic information such as PAVM location and size, which are critical for treatment decision and planning. They also may remain positive after successful coil embolization.
- Although MRA lacks the spatial resolution of CT, it has an important role given the lack of ionizing radiation and need for repeat lifelong examinations in patients with HHT potentially starting at a young age.
- Diagnostic PA remains the reference standard for inconclusive cases and remains a critical component of the treatment of PAVMs when performed with concurrent transcatheter embolization.

**Summary of Evidence**

Of the 21 references cited in the *ACR Appropriateness Criteria® Clinically Suspected Pulmonary Arteriovenous Malformation* document, all of them are categorized as diagnostic references including 1 well designed study, 2 good quality studies, and 7 quality studies that may have design limitations. There are 10 references that may not be useful as primary evidence. There is 1 reference that is a meta-analysis study.

The 21 references cited in the *ACR Appropriateness Criteria® Clinically Suspected Pulmonary Arteriovenous Malformation document* were published from 1992-2015.

While there are references that report on studies with design limitations, 3 well designed or good quality studies provide good evidence.
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, both because of 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 to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document.

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<tr>
<th>Relative Radiation Level*</th>
<th>Adult Effective Dose Estimate Range</th>
<th>Pediatric Effective Dose Estimate Range</th>
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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient’s clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient’s condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.