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iREVIEWS

STATE-OF-THE-ART PAPER

Imaging in Pulmonary Hypertension

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Pulmonary hypertension is defined as an increase in mean pulmonary arterial pressure ≥25 mm Hg at rest and occurs in a majority of patients with heart failure. Diagnostic imaging targets the right ventricle and the pulmonary vasculature. Although echocardiography is cost-effective for screening and follow-up, right heart catheterization is still mandatory to differentiate pre- from post-capillary disease and to directly measure pressure and flow. An important goal is to rule out chronic thromboembolic pulmonary hypertension. This diagnostic step can be achieved by perfusion scintigraphy, whereas computed tomography and cardiac magnetic resonance have become indispensable ancillary methods for the diagnostic allocation to other World Health Organization subtypes of pulmonary hypertension. (J Am Coll Cardiol Img 2010;3:1287–95) © 2010 by the American College of Cardiology Foundation

Pulmonary hypertension is a hemodynamic and pathophysiological state that can be found in multiple clinical conditions and is defined as an invasively measured mean pulmonary arterial pressure ≥25 mm Hg at rest (1). The fourth World Health Organization Symposium on Pulmonary Hypertension in Dana Point, California, in 2008 provided an updated classification (2) and recommendations for contemporary diagnosis and treatment (3). Five subsets have been defined: group 1 as pulmonary arterial hypertension (PAH), group 2 as pulmonary hypertension due to left heart disease, group 3 as pulmonary hypertension due to lung diseases and/or hypoxia, group 4 as chronic thromboembolic pulmonary hypertension (1), and group 5 as pulmonary hypertension of other causes. Pulmonary arterial hypertension is a rapidly progressive and fatal disease leading to right ventricular (RV) failure and death (4). Prognosis is dependent on disease subtype, sex, renal function, hemodynamics, World Health Organization functional class, exercise capacity, brain natriuretic peptide levels, pericardial effusion by echocardiography, diffusion capacity for carbon monoxide, and vital parameters at diagnosis (5,6). Incidences are assumed to be as low as 2.4 cases per million for PAH and as high as 60% to 70% of all cases with systolic and/or diastolic left ventricular dysfunction. An invasively measured resting pulmonary capillary wedge pressure of 15 mm Hg has been used to distinguish between pre- and post-capillary pulmonary hypertension. This distinction is critical because post-capillary pulmonary hypertension does not respond to treatments for pre-capillary pulmonary hypertension. Hence, when invasive pressure measurements are performed during right heart catheterization, capillary wedge pressure measurements must be

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exact, and because of the frequent technical difficulties encountered when trying to obtain reliable wedge curves, left ventricular end-diastolic pressure should be documented in parallel. Post-capillary pulmonary hypertension (7) is an important subset and accounts for 50% of all cardiac complications and 19% of early deaths in a heart failure population (8,9).

The early clinical signs and symptoms are scarce, and the majority of patients have advanced disease with World Health Organization functional classes higher than III at first presentation (10). PAH should be considered in the differential diagnosis of unexplained fatigue, exertional dyspnea, syncope, angina, and progressive limitation of exercise capacity, particularly in patients without common cardiovascular or respiratory disorders.

The goal of imaging in pulmonary hypertension is to establish the diagnosis and identify disease subsets. Because the main anatomic components of the pulmonary circulation are the RV and the pulmonary vasculature, those are addressed separately in this review.

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

CT = computed tomography

PAH = pulmonary arterial hypertension

RV = right ventricular

V/Q = radionuclide ventilation-perfusion scanning

Imaging of the Right Ventricle

RV function is affected at rest when >50% of pulmonary resistance vessels are dysfunctional (11,12). RV function is important because it is a predictor of survival (1,4,13). Due to its shape and location and the load dependence of the ejection fraction, accurate evaluation of RV function remains challenging. The ultimate goal of imaging of the RV is to replace invasive right heart catheterization, which is currently the gold standard for assessing filling pressures, compartmental saturations, and parameters of RV function.

Echocardiography. Cutoffs for simple and advanced echocardiographic techniques for the diagnosis and follow-up of pulmonary hypertension are summarized in Tables 1 (14–20) and 2 (21–26). RV function reflects mechanical coupling between the right ventricle and the pulmonary artery (27). An enlarged right ventricle may result from volume overload or intrinsic systolic or diastolic dysfunction or may be a sign of manifest pulmonary hypertension. Transthoracic echocardiography and Doppler imaging provide direct and easily accessible important information on relative chamber sizes, left and right ventricular function and valvular abnormalities; permit estimation of RV hemodynamics; and are therefore essential for the workup of suspected pulmonary hypertension. The peak pressure gradient of tricuspid insufficiency is calculated as 4 × (Doppler imaging–derived maximal tricuspid regurgitation velocity in meters) squared. Based on this result, systolic pulmonary arterial pressure is estimated by adding the estimated right atrial pressure in millimeters of mercury (mm Hg). Correlations between echocardiography/Doppler imaging and invasive measurements of systolic pulmonary arterial pressure are high, with r values ranging from 0.57 to 0.93 (3). An estimated systolic pulmonary arterial pressure of >50 mm Hg has been set as an arbitrary cutoff in symptomatic patients to justify invasive evaluation (3) (Table 1).

Although several further Doppler imaging–based calculations have been proposed (28), none of them, including estimates of pulmonary vascular resistance (29,30) (Table 2), has yet helped circumvent invasive evaluations. However, the presence of a pericardial effusion has been confirmed as a predictor of outcome (6,31). In addition, echocardiographic parameters allow monitoring of medical treatment (32) or outcomes after pulmonary endarterectomy (33). Recent data (34) suggest that diminished systolic longitudinal deformation reflects the degree of RV dysfunction (Fig. 1, Online Videos 1 to 4). Three-dimensional (3D) echocardiography shows promise for measuring RV volumes and function compared with cardiac magnetic resonance (CMR) (35), but more experience is needed.

CMR. The current diagnostic value of CMR was recently critically reviewed (36). CMR provides information on RV size, morphology and function, interventricular septal configuration, volumes and mass, and the left-right delay in myocardial shortening (37) and permits the direct assessment of forward and regurgitant flow, stroke volume, pulmonary arterial distensibility, and RV mass (38,39). Increased RV end-diastolic volume may be the most appropriate marker for progressive RV failure (40). The reproducibility of CMR-derived parameters of ventricular function and mass is superior to 2-dimensional echocardiography (41) and makes CMR useful for follow-up.

Imaging of the Pulmonary Vasculature

Chest X-ray. Although of low sensitivity and specificity, a plain chest X-ray film can reveal significant pulmonary vascular pathology (42) by illustrating vessel displacement and hyper- or hypovascularity of the lungs.

Table 1. Comparison of Cutoffs of Simple Echocardiographic Measurements for the Diagnosis and Follow-Up of Pulmonary Hypertension

Echocardiographic Measurement	Cutoff	Added Value	Ref. #
Peak velocity of tricuspid regurgitation	>3.4 m/s >2.9 m/s	Predictor of sPAP >50 mm Hg Predictor of sPAP >40 mm Hg	3, 14, 15
Pulmonary flow acceleration time of RV ejection into the pulmonary artery	<93 ms	Diagnosis of PH	16,17,18
Tricuspid annular plane systolic excursion	<18 mm	Estimate of significant RV systolic dysfunction and predictor of prognosis	19
Tricuspid annular tissue Doppler systolic velocity	<12 cm/s <10 cm/s	Predictor of sPAP >40 mm Hg Predictor of PVR >1,000 dyne/s/cm^{-5}	20, 30

PH = pulmonary hypertension; PVR = pulmonary vascular resistance; RV = right ventricular; sPAP = systolic pulmonary arterial pressure.

Radioisotope ventilation–perfusion scanning. For diagnosis of acute pulmonary embolism (43), computed tomography (CT) is the widely accepted method of choice and has largely replaced planar radionuclide ventilation-perfusion scanning (V/Q). By contrast, V/Q is the main imaging modality to look for chronic thromboembolic pulmonary hypertension (7) (Fig. 2) (44) because of its superior sensitivity compared with that of CT (45–49) (Table 3). The criterion with which to diagnose chronic thromboembolic pulmonary hypertension on a V/Q scan is at least 1 larger defect (i.e., composing at least half a segment) after a minimum of 3 months of effective anticoagulation. V/Q has 90% to 100% sensitivity and 94% to 100% specificity for the diagnosis (Table 3). Potential pitfalls are small, matched defects or nonsegmental perfusion abnormalities as they occur in PAH and pulmonary veno-occlusive disease (1,50,51) (Figs. 3C and 3D). Furthermore, the classic segmental perfusion defects may disappear in end-stage chronic thromboembolic pulmonary hypertension (52). In nonthromboembolic pulmonary hypertension, nonhomogeneous, patchy perfusion abnormalities typically lack a lobar or segmental distribution (Fig. 3D). In cases of large central thrombi of Eisenmenger syndrome or in cases of thrombi within major vessel pulmonary arterial aneurysms of severe idiopathic PAH, perfusion scintigrams remain nonsegmental (53).

Pulmonary angiography. Pulmonary angiography can be performed safely (54). Because of its supreme ability to visualize even small pulmonary arteries, pulmonary angiography is the gold standard of imaging thrombotic occlusions (Fig. 3 and Online

Table 2. Comparison of Cutoffs of Advanced Echocardiographic Techniques for the Diagnosis and Follow-Up of Pulmonary Hypertension

Echocardiographic Measurement	Cutoff	Added Value	Ref. #
Tricuspid annular DTI velocity time integral	≤2.5 cm	Predictor of sPAP >40 mm Hg	20
Continuous or pulsed Doppler of pulmonary regurgitation	$4 \times V^2 + RAP$	For estimation of mean pulmonary arterial pressure	34
sHVF	sHVF VTI/(sHVF VTI + dHVF VTI) <55%	Predictor of right atrial pressure >8 mm Hg	21
RV myocardial performance index (Tei index) (IVRT + IVCT)/RVET	>0.36	Predictor of mPAP >25 mm Hg	22
Pulmonary vascular capacitance (stroke volume/pulse pressure)	<3.0 ml/mm Hg decrease	Predictor of poor prognosis	23
2-dimensional strain of the basal segment of the RV free wall	<10% systolic longitudinal deformation	Predictor of poor prognosis	34
GPSS and LPSS	Decrease in RV ejection fraction by 1%	Decrease in GPSS by 14%, and LPSS of RV free wall by 27%	24
(Pulmonary ejection period/pulmonary acceleration time) divided by RV total systolic time	>2.6	Predictor of PVR >2.5 Wood units	25
Pulsed Doppler early diastolic tricuspid inflow/tissue Doppler early diastolic myocardial velocity at the tricuspid lateral annulus E_{Tr}/E'_{Tr}	>6	Predictor of mean RAP ≥10 mm Hg	26

dHVF = diastolic hepatic venous flow; DTI = Doppler tissue imaging; GPSS = global peak systolic strain; IVCT = isovolumetric contraction time; IVRT = isovolumetric relaxation time; LPSS = longitudinal peak systolic strain; mPAP = mean pulmonary artery pressure; RAP = right atrial pressure; RVET = right ventricular ejection time; sHVF = systolic hepatic venous flow; VTI = velocity time integral; other abbreviations as in Table 1.

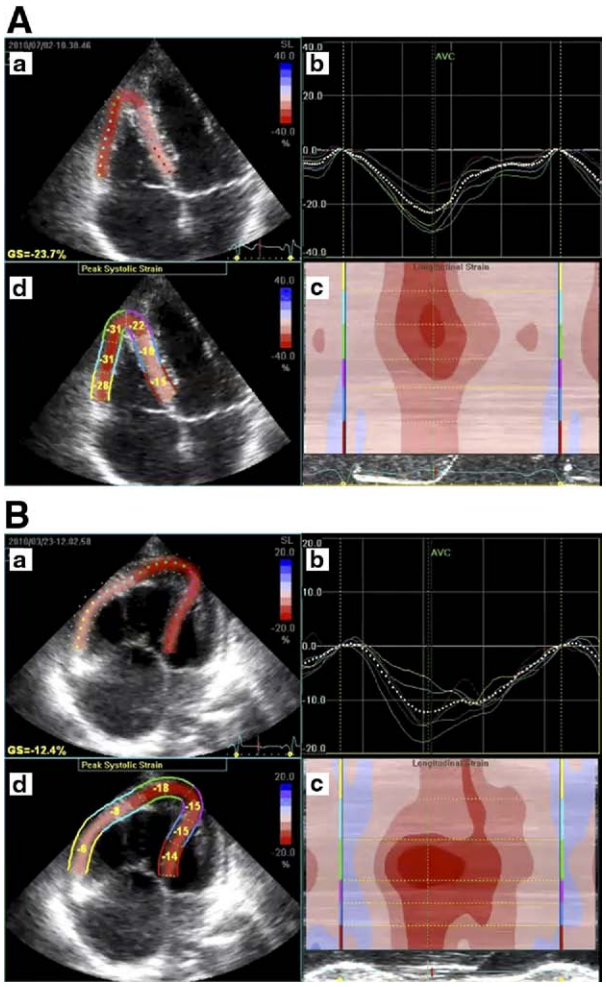

Figure 1. Longitudinal Strain Analysis Using Speckle Tracking

(A) Subject with normal pulmonary artery pressures and normal right ventricular (RV) function and **(B)** patient with severe pulmonary hypertension and reduced RV function. **(Aa, Ba)** RV function using peak systolic longitudinal strain. Darker shades of red denote regions of better longitudinal function. **(Ab, Bb)** Corresponding strain curves. **(Ac, Bc)** Curved M- mode of peak systolic strain. **(Ad, Bd)** Segmental values for peak longitudinal systolic strain (%) of the right ventricle. See Online Videos 1, 2, 3, and 4.

Videos 5 to 12). Although the magnitude of perfusion defects generally leads to an underestimation of vascular obstruction in chronic thromboembolic pulmonary hypertension, angiography is generally able to depict thrombus at the subsegmental and segmental levels, which is one of the criteria for operability.

Multislice CT. Contrast CT angiography including 3D rendering techniques shows whether arteries or veins are primarily affected (Figs. 3A vs. 3C), and depicts webs and bands, wall irregularities, stenoses, aneurysms, and complete vascular obstructions, as well as bronchial collaterals (55). Bronchial artery enlargement has been positively correlated with disease burden in chronic thromboembolic disease (56), but is not a reliable diagnostic criterion. CT angiography may help detect rare structural problems resulting from pulmonary hypertension, such as aneurysms and dissections of pulmonary arteries, as they may occur in Eisenmenger syndrome or schistosomiasis, and left main coronary artery compression by a large pulmonary artery (57).

High-resolution CT delivers images of the lung parenchyma, allows exclusion of emphysema, bronchitis, and interstitial lung disease as well as infarcts, vascular and pericardial malformations, and thoracic wall deformities. High-resolution CT may be helpful for the diagnosis of pulmonary veno-occlusive disease with ground-glass opacities, interstitial edema, and bilateral thickenings of the interlobular septae (58,59) (Fig. 3C). Perfusion inequalities, such as a sequela of chronic thrombotic pulmonary artery occlusion (60) and other lung disease (61), manifest as a mosaic parenchymal pattern with dark areas corresponding to relatively decreased perfusion. Although a mosaic pattern is more common in chronic thromboembolic pulmonary hypertension, it is observed in as many as 12% of patients with PAH (62). Exhalation sequences can help exclude pulmonary vascular disease with accentuation of the darker regions of air trapping in small airways disease.

CMR. CMR of the pulmonary vasculature is becoming increasingly useful (63). Techniques include 2- and 3D contrast-enhanced CMR angiography, CMR perfusion (64,65), and phase-contrast imaging. One area of investigation is circulatory changes in the proximal pulmonary artery. Main pulmonary artery blood flow velocity at peak systole, maximal systolic main pulmonary artery cross-sectional area, and patient height and weight have been used to calculate pulmonary arterial pressure (66). Main pulmonary artery area distensibility and relative area

Table 3. Accuracy of Various Imaging Methods Against Pulmonary Angiography as the Reference Method to Diagnose Chronic Thromboembolic Pulmonary Hypertension

Method	Ref. #	Sensitivity, %	Specificity, %
V/Q	46	90.0–100.0	94.0–100.0
	45	96.0–97.4	90.0–95.0
	47	100.0	86.0
CT	45	51.3	99.0
	60	97.0	79.3
	48	98.3/94.1	94.8
CMR	49	80.0	93.0

CMR = cardiac magnetic resonance; CT = computed tomography; V/Q = radionuclide ventilation-perfusion scanning.

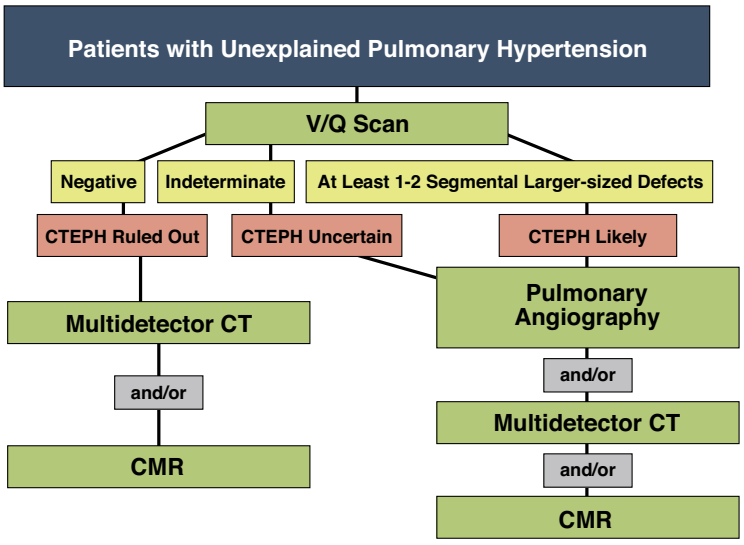

Figure 2. Contemporary Diagnostic Imaging Algorithm

Radionuclide ventilation-perfusion scanning (V/Q) plays a key role in ruling out chronic thromboembolic pulmonary hypertension (44). Due to wider availability and more evidence, computed tomography (CT) has been ranked before cardiac magnetic resonance (CMR) (3). Center-specific use of imaging modalities may vary. CTEPH = chronic thromboembolic pulmonary hypertension.

change, calculated as relative cross-sectional area change, predict mortality in patients with PAH (63).

At present, only limited evidence exists in support of either CT or magnetic resonance angiography for definition of thromboembolic obstructions in chronic thromboembolic pulmonary hypertension (Table 3) (67,68).

Coronary angiography. Conventional coronary angiography has become an important component of diagnostic pulmonary hypertension imaging because of surgical treatment options, an increasingly comorbid patient population, and a significant likelihood of coronary artery disease in the Western population. Late-generation CT coronary imaging may replace invasive coronary angiographies in suitable patients (69). Anatomic distortions due to right heart enlargement and coronary-to-pulmonary anastomoses are common.

Current Recommendations

In most instances, echocardiography is the initial tool to suspect pulmonary hypertension; nevertheless, invasive measurements remain indispensible for the diagnosis and assessment of pulmonary vascular reactivity (3). V/Q is a reliable and cost-effective strategy to rule out chronic thromboembolic pulmonary hypertension. Starting out with V/Q (Fig. 2) may save the patient an additional catheterization procedure because hemodynamic measurements can be performed concurrent with pulmonary angiography. CT and/or CMR are used as subsequent diagnostic imaging steps. Follow-up is accomplished by echocardiography, CMR, and right heart catheterizations.

The Future of Imaging in Pulmonary Hypertension

Accurate visualization of complex RV anatomies by advanced imaging techniques and precise measurement of blood volumes and flow may obviate invasive procedures in the future (70). In addition, current concepts suggest that pathological remodeling occurs at the level of the pulmonary resistance vessels measuring approximately 100 μm in diameter. If one were able to visualize these small vessels, recognize occlusions, and ultimately also identify hypertrophy of the smooth muscle cell layer, one might be able to predict the development of pulmonary hypertension at early stages when hemodynamics are still normal. Although current CT technology captures structures as small as 1,000 μm, phase contrast CT depicts vessels in the range of 100 μm. Thus, early disease recognition is one of the main challenges for future imaging. Such early recognition may allow for earlier preventive and therapeutic approaches (71), which could ultimately change the incidence and clinical manifestations of pulmonary hypertension as we know it today (66).

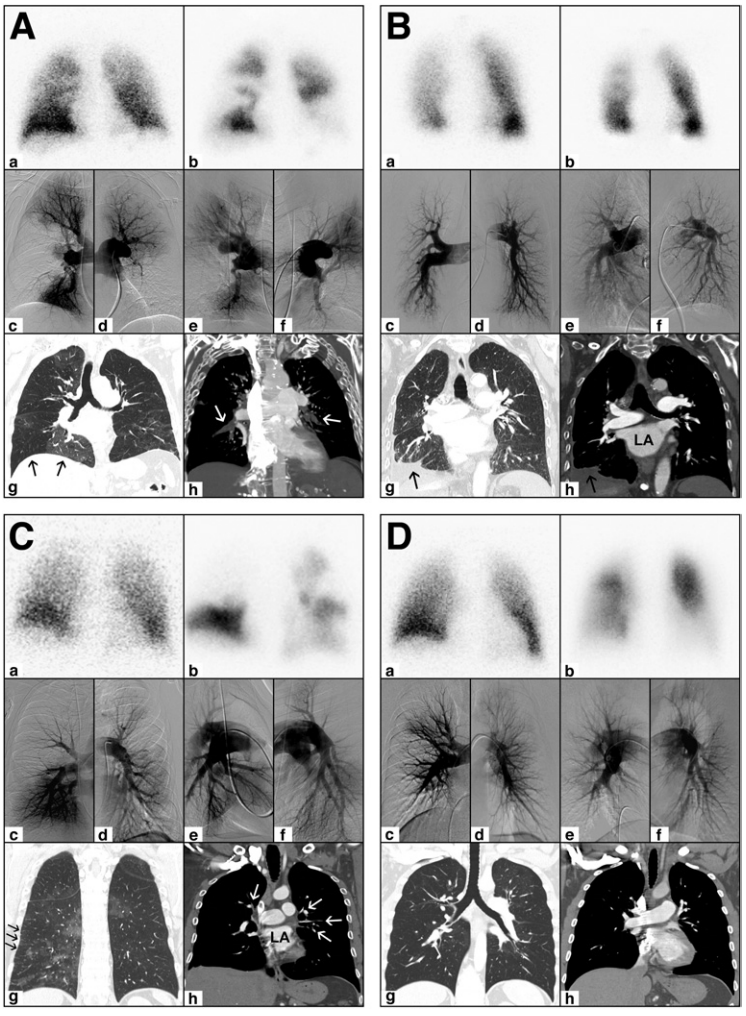

Figure 3. Completed Diagnostic Pathway of PAH Imaging Following the Diagnostic Algorithm Shown in Figure 2

(Aa, Ab, Ba, Bb, Ca, Cb) Examples of radionuclide ventilation-perfusion scanning (V/Q) labeled high probability under PIOPED criteria. In contrast, low-probability V/Q of an idiopathic pulmonary arterial hypertension (PAH) case and corresponding diagnostic images are shown **(Da, Db)**. **(a)** Technetium-99m–labeled aerosol ventilation images are shown. **(b)** Technetium-99m–labeled macroaggregated human albumin injected perfusion images. **(Ac–Af, Bc–Bf, Cc–Cf, Dc–Df)** Classic side-selective pulmonary angiography in the anteroposterior and lateral projections. Pulmonary angiograms were captured at frames that allow assessment of early capillary filling. The respective anterior-posterior views of the pulmonary angiograms are also provided as Online Videos (Online Videos 5, 6, 7, 8, 9, 10, 11, and 12). High-resolution computed tomography (CT) **(Ag, Bg, Cg, Dg)** and spiral CT angiography **(Ah, Bh, Ch, Dh)**. **(A)** Images of a 65-year-old patient with chronic thromboembolic pulmonary hypertension. Based on central thrombus location and a pulmonary arterial pressure of 70/27/45 mm Hg, with a cardiac output of 3.7 l/min, the patient was judged operable. **Arrows** indicate perfused lung tissue (bright opacification), contrasting with unperfused areas (dark opacification, mosaic perfusion pattern **(Ag)**. **White arrows** highlight fresh thrombus at the lower lobe artery take-offs **(Ah). (B)** Images of a 78-year-old female patient with chronic obstructive pulmonary disease Gold stage III. Invasive pressure measurements demonstrated elevated pulmonary arterial pressures of 115/44/68 mm Hg, with a cardiac output of 3.2 l/min. Despite a high-probability V/Q **(Ba, Bb)**, pulmonary angiography was completely normal **(Bc to Bf)**. Right lower lobe attenuation was due to atelectasis of part of the lower lobe and pleural effusion **(Bg, Bh, arrows)**. **(C)** Images of a 52-year-old male patient with pulmonary veno-occlusive disease. Invasive pressure measurements demonstrated mildly elevated pulmonary arterial pressures of 49/25/38 mm Hg, with a cardiac output of 4.7 l/min. As substrate for the high-probability lung perfusion scan **(Ca, Cb)**, pulmonary angiography showed a territorial lack of the capillary filling phase **(Cc–Cf)**. Pulmonary arteries were narrow but smooth. **Arrows** indicate Kerley B lines **(Cg)**. **White arrows** point to obliterated pulmonary veins close to the entry into the left atrium **(Ch)**. **(D)** Images of a 47-year-old male patient with idiopathic PAH. Invasive pressure measurements demonstrated pulmonary arterial pressures of 59/22/36 mm Hg, with a cardiac output of 4.23 l/min (cardiac index of 1.5 l/min/m^2). **(Da, Db)** Low-probability lung V/Q with some nonsegmental patchiness on perfusion **(Db)**. High-probability scans have been reported in 0.01% of PAH cases (45). Although perfusion scans in idiopathic PAH may show certain abnormalities, the presence of ≥1 segmental or larger perfusion defects should suggest the diagnosis of potentially correctable, major-vessel chronic thromboembolic pulmonary hypertension. Note the pruning of peripheral pulmonary arteries **(Dc to Df)**. No mosaic pattern was seen by high-resolution CT **(Dg)**.

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REFERENCES

1. Badesch DB, Champion HC, Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. J Am Coll Cardiol 2009; 54:S55–66.
2. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol 2009;54:S43–54.
3. Galie N, Hoeper MM, Humbert M, et al. Guidelines for the diagnosis and treatment of pulmonary hypertension: The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). Eur Heart J 2009;30:2493–537.
4. D'Alonzo GE, Barst RJ, Ayres SM, et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. Ann Intern Med 1991;115:343–9.
5. Humbert M, Sitbon O, Yaici A, et al. Survival in incident and prevalent cohorts of patients with pulmonary arterial hypertension. Eur Respir J 2010; 36:549–55.
6. Benza RL, Miller DP, Gomberg-Maitland M, et al. Predicting survival in pulmonary arterial hypertension: insights from the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL). Circulation 2010;122: 164–72.
7. Hoeper MM, Barbera JA, Channick RN, et al. Diagnosis, assessment, and treatment of non-pulmonary arterial hypertension pulmonary hypertension. J Am Coll Cardiol 2009;54:S85–96.
8. Hosenpud JD, Bennett LE, Keck BM, Boucek MM, Novick RJ. The Registry of the International Society for Heart and Lung Transplantation: seventeenth official report-2000. J Heart Lung Transplant 2000;19:909–31.
9. Lam CS, Roger VL, Rodeheffer RJ, Borlaug BA, Enders FT, Redfield MM. Pulmonary hypertension in heart failure with preserved ejection fraction: a community-based study. J Am Coll Cardiol 2009;53:1119–26.
10. Humbert M, Sitbon O, Chaouat A, et al. Pulmonary arterial hypertension in France: results from a national registry. Am J Respir Crit Care Med 2006; 173:1023–30.
11. Sharma GV, McIntyre KM, Sharma S, Sasahara AA. Clinical and hemodynamic correlates in pulmonary embolism. Clin Chest Med 1984;5:421–37.
12. Harris P, Segel N, Bishop JM. The relation between pressure and flow in the pulmonary circulation in normal subjects and in patients with chronic bronchitis and mitral stenosis. Cardiovasc Res 1968;2:73–83.
13. Thenappan T, Shah SJ, Rich S, Tian L, Archer SL, Gomberg-Maitland M. Survival in pulmonary arterial hypertension: a reappraisal of the NIH risk stratification equation. Eur Respir J 2010;35:1079–87.
14. Mukerjee D, St George D, Knight C, et al. Echocardiography and pulmonary function as screening tests for pulmonary arterial hypertension in systemic sclerosis. Rheumatology (Oxford) 2004;43:461–6.
15. Grunig E, Janssen B, Mereles D, et al. Abnormal pulmonary artery pressure response in asymptomatic carriers of primary pulmonary hypertension gene. Circulation 2000;102:1145–50.
16. Lanzarini L, Fontana A, Campana C, Klersy C. Two simple echo-Doppler measurements can accurately identify pulmonary hypertension in the large majority of patients with chronic heart failure. J Heart Lung Transplant 2005;24:745–54.
17. Naeije R, Torbicki A. More on the noninvasive diagnosis of pulmonary hypertension: Doppler echocardiography revisited. Eur Respir J 1995;8:1445–9.
18. Lopez-Candales A, Eleswarapu A, Shaver J, Edelman K, Gulyasy B, Candales MD. Right ventricular outflow tract spectral signal: a useful marker of right ventricular systolic performance and pulmonary hypertension severity. Eur J Echocardiogr 2010;11:509–15.
19. Forfia PR, Fisher MR, Mathai SC, et al. Tricuspid annular displacement predicts survival in pulmonary hypertension. Am J Respir Crit Care Med 2006;174:1034–41.
20. Melek M, Esen O, Esen AM, et al. Tissue Doppler evaluation of tricuspid annulus for estimation of pulmonary artery pressure in patients with COPD. Lung 2006;184:121–31.
21. Nageh MF, Kopelen HA, Zoghbi WA, Quinones MA, Nagueh SF. Estimation of mean right atrial pressure using tissue Doppler imaging. Am J Cardiol 1999;84:1448–51, A8.
22. Blanchard DG, Malouf PJ, Gurudevan SV, et al. Utility of right ventricular Tei index in the noninvasive evaluation of chronic thromboembolic pulmonary hypertension before and after pulmonary thromboendarterectomy. J Am Coll Cardiol Img 2009;2:143–9.
23. Mahapatra S, Nishimura RA, Oh JK, McGoon MD. The prognostic value of pulmonary vascular capacitance determined by Doppler echocardiography in patients with pulmonary arterial hypertension. J Am Soc Echocardiogr 2006;19:1045–50.
24. Scherptong RW, Mollema SA, Blom NA, et al. Right ventricular peak systolic longitudinal strain is a sensitive marker for right ventricular deterioration in adult patients with tetralogy of Fallot. Int J Cardiovasc Imaging 2009;25: 669–76.
25. Scapellato F, Temporelli PL, Eleuteri E, Corra U, Imparato A, Giannuzzi P. Accurate noninvasive estimation of pulmonary vascular resistance by Doppler echocardiography in patients with chronic failure heart failure. J Am Coll Cardiol 2001;37:1813–9.
26. Utsunomiya H, Nakatani S, Nishihira M, et al. Value of estimated right ventricular filling pressure in predicting cardiac events in chronic pulmonary arterial hypertension. J Am Soc Echocardiogr 2009;22:1368–74.
27. Chesler NC, Roldan A, Vanderpool RR, Naeije R. How to measure pulmonary vascular and right ventricular function. Conf Proc IEEE Eng Med Biol Soc 2009;2009:177–80.
28. Chemla D, Castelain V, Provencher S, Humbert M, Simonneau G, Herve P. Evaluation of various empirical formulas for estimating mean pulmonary artery pressure by using systolic pulmonary artery pressure in adults. Chest 2009;135:760–8.
29. Vlahos AP, Feinstein JA, Schiller NB, Silverman NH. Extension of Doppler-derived echocardiographic measures of pulmonary vascular resistance to patients with moderate or severe pulmonary vascular disease. J Am Soc Echocardiogr 2008;21:711–4.

30. Gurudevan SV, Malouf PJ, Auger WR, et al. Abnormal left ventricular diastolic filling in chronic thromboembolic pulmonary hypertension: true diastolic dysfunction or left ventricular underfilling? J Am Coll Cardiol 2007; 49:1334–9.
31. Raymond RJ, Hinderliter AL, Willis PW, et al. Echocardiographic predictors of adverse outcomes in primary pulmonary hypertension. J Am Coll Cardiol 2002;39:1214–9.
32. Galie N, Hinderliter AL, Torbicki A, et al. Effects of the oral endothelin-receptor antagonist bosentan on echocardiographic and Doppler measures in patients with pulmonary arterial hypertension. J Am Coll Cardiol 2003;41:1380–6.
33. Reesink HJ, Marcus JT, Tulevski, II, et al. Reverse right ventricular remodeling after pulmonary endarterectomy in patients with chronic thromboembolic pulmonary hypertension: utility of magnetic resonance imaging to demonstrate restoration of the right ventricle. J Thorac Cardiovasc Surg 2007;133:58–64.
34. Borges AC, Knebel F, Eddicks S, et al. Right ventricular function assessed by two-dimensional strain and tissue Doppler echocardiography in patients with pulmonary arterial hypertension and effect of vasodilator therapy. Am J Cardiol 2006;98:530–4.
35. Grapsa J, O'Regan DP, Pavlopoulos H, Durighel G, Dawson D, Nihoyannopoulos P. Right ventricular remodelling in pulmonary arterial hypertension with three-dimensional echocardiography: comparison with cardiac magnetic resonance imaging. Eur J Echocardiogr 2010;11:64–73.
36. Benza R, Biederman R, Murali S, Gupta H. Role of cardiac magnetic resonance imaging in the management of patients with pulmonary arterial hypertension. J Am Coll Cardiol 2008;52:1683–92.
37. Marcus JT, Gan CT, Zwanenburg JJ, et al. Interventricular mechanical asynchrony in pulmonary arterial hypertension: left-to-right delay in peak shortening is related to right ventricular overload and left ventricular underfilling. J Am Coll Cardiol 2008;51: 750–7.
38. Torbicki A. Cardiac magnetic resonance in pulmonary arterial hypertension: a step in the right direction. Eur Heart J 2007;28:1187–9.
39. van Wolferen SA, Marcus JT, Boonstra A, et al. Prognostic value of right ventricular mass, volume, and function in idiopathic pulmonary arterial hypertension. Eur Heart J 2007;28: 1250–7.
40. Gan CT, Holverda S, Marcus JT, et al. Right ventricular diastolic dysfunction and the acute effects of sildenafil in pulmonary hypertension patients. Chest 2007;132:11–7.
41. Grothues F, Smith GC, Moon JC, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 2002;90:29–34.
42. Kerr IH. Vascular changes in the lungs on the plain radiograph of the chest. Postgrad Med J 1970;46:3–10.
43. Ceriani E, Combescure C, Le Gal G, et al. Clinical prediction rules for pulmonary embolism: a systematic review and meta-analysis. J Thromb Haemost 2010;8:957–70.
44. Keogh AM, Mayer E, Benza RL, et al. Interventional and surgical modalities of treatment in pulmonary hypertension. J Am Coll Cardiol 2009;54: S67–77.
45. Tunariu N, Gibbs SJ, Win Z, et al. Ventilation-perfusion scintigraphy is more sensitive than multidetector CTPA in detecting chronic thromboembolic pulmonary disease as a treatable cause of pulmonary hypertension. J Nucl Med 2007;48:680–4.
46. Fedullo PF, Auger WR, Kerr KM, Rubin LJ. Chronic thromboembolic pulmonary hypertension. N Engl J Med 2001;345:1465–72.
47. Worsley DF, Palevsky HI, Alavi A. Ventilation-perfusion lung scanning in the evaluation of pulmonary hypertension. J Nucl Med 1994;35:793–6.
48. Reichelt A, Hoeper MM, Galanski M, Keberle M. Chronic thromboembolic pulmonary hypertension: evaluation with 64-detector row CT versus digital substraction angiography. Eur J Radiol 2009;71:49–54.
49. Nikolaou K, Schoenberg SO, Attenberger U, et al. Pulmonary arterial hypertension: diagnosis with fast perfusion MR imaging and high-spatial-resolution MR angiography—preliminary experience. Radiology 2005;236:694–703.
50. Rush C, Langleben D, Schlesinger RD, Stern J, Wang NS, Lamoureux E. Lung scintigraphy in pulmonary capillary hemangiomatosis. A rare disorder causing primary pulmonary hypertension. Clin Nucl Med 1991;16:913–7.
51. Bailey CL, Channick RN, Auger WR, et al. "High probability" perfusion lung scans in pulmonary venoocclusive disease. Am J Respir Crit Care Med 2000;162:1974–8.
52. Skoro-Sajer N, Becherer A, Klepetko W, Kneussl MP, Maurer G, Lang IM. Longitudinal analysis of perfusion lung scintigrams of patients with unoperated chronic thromboembolic pulmonary hypertension. Thromb Haemost 2004;92:201–7.
53. Moser KM, Fedullo PF, Finkbeiner WE, Golden J. Do patients with primary pulmonary hypertension develop extensive central thrombi? Circulation 1995;91:741–5.
54. Pitton MB, Duber C, Mayer E, Thelen M. Hemodynamic effects of nonionic contrast bolus injection and oxygen inhalation during pulmonary angiography in patients with chronic major-vessel thromboembolic pulmonary hypertension. Circulation 1996; 94:2485–91.
55. Cummings KW, Bhalla S. Multidetector computed tomographic pulmonary angiography: beyond acute pulmonary embolism. Radiol Clin North Am 2010;48:51–65.
56. Shimizu H, Tanabe N, Terada J, et al. Dilatation of bronchial arteries correlates with extent of central disease in patients with chronic thromboembolic pulmonary hypertension. Circ J 2008; 72:1136–41.
57. Bonderman D, Fleischmann D, Prokop M, Klepetko W, Lang IM. Images in cardiovascular medicine. Left main coronary artery compression by the pulmonary trunk in pulmonary hypertension. Circulation 2002;105:265.
58. Dufour B, Maitre S, Humbert M, Capron F, Simonneau G, Musset D. High-resolution CT of the chest in four patients with pulmonary capillary hemangiomatosis or pulmonary venoocclusive disease. AJR Am J Roentgenol 1998;171:1321–4.
59. Montani D, Achouh L, Sitbon O, Simonneau G, Humbert M. Pulmonary venoocclusive disease and failure of specific therapy. Chest 2009;136: 1181, author reply 1181–2.
60. Bergin CJ, Rios G, King MA, Belezzuoli E, Luna J, Auger WR. Accuracy of high-resolution CT in identifying chronic pulmonary thromboembolic disease. AJR Am J Roentgenol 1996; 166:1371–7.
61. Stern EJ, Swensen SJ, Hartman TE, Frank MS. CT mosaic pattern of lung attenuation: distinguishing different causes. AJR Am J Roentgenol 1995; 165:813–6.
62. Sherrick AD, Swensen SJ, Hartman TE. Mosaic pattern of lung attenuation on CT scans: frequency among patients with pulmonary artery hypertension of different causes. AJR Am J Roentgenol 1997;169:79–82.
63. Gan CT, Lankhaar JW, Westerhof N, et al. Noninvasively assessed pulmonary artery stiffness predicts mortality in pulmonary arterial hypertension. Chest 2007;132:1906–12.

64. Amundsen T, Torheim G, Kvistad KA, et al. Perfusion abnormalities in pulmonary embolism studied with perfusion MRI and ventilation-perfusion scintigraphy: an intra-modality and inter-modality agreement study. J Magn Reson Imaging 2002;15:386–94.
65. Ley S, Kauczor HU. MR imaging/magnetic resonance angiography of the pulmonary arteries and pulmonary thromboembolic disease. Magn Reson Imaging Clin N Am 2008;16:263–73, ix.
66. Laffon E, Vallet C, Bernard V, et al. A computed method for noninvasive MRI assessment of pulmonary arterial hypertension. J Appl Physiol 2004;96:463–8.
67. Bergin CJ, Sirlin CB, Hauschildt JP, et al. Chronic thromboembolism: diagnosis with helical CT and MR imaging with angiographic and surgical correlation. Radiology 1997;204:695–702.
68. Kreitner KF, Ley S, Kauczor HU, et al. Chronic thromboembolic pulmonary hypertension: pre- and postoperative assessment with breath-hold MR imaging techniques. Radiology 2004;232:535–43.
69. Nicol ED, Kafka H, Stirrup J, et al. A single, comprehensive non-invasive cardiovascular assessment in pulmonary arterial hypertension: combined computed tomography pulmonary and coronary angiography. Int J Cardiol 2009;136:278–88.
70. Nogami M, Ohno Y, Koyama H, et al. Utility of phase contrast MR imaging for assessment of pulmonary flow and pressure estimation in patients with pulmonary hypertension: comparison with right heart catheterization and echocardiography. J Magn Reson Imaging 2009;30:973–80.
71. Galie N, Rubin L, Hoeper M, et al. Treatment of patients with mildly symptomatic pulmonary arterial hypertension with bosentan (EARLY study): a double-blind, randomised controlled trial. Lancet 2008;371:2093–100.

Key Words: perfusion scintigraphy ■ pulmonary hypertension ■ pulmonary vascular resistance ■ right ventricle.

APPENDIX

For supplemental videos, please see the online version of this article.