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STATE-OF-THE-ART PAPER

Role of Cardiac Magnetic Resonance Imaging in the Management of Patients With Pulmonary Arterial Hypertension

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Pulmonary arterial hypertension (PAH) is a progressive disorder characterized by abnormally elevated blood pressure of the pulmonary circulation that results, over time, from extensive vascular remodeling and increased pulmonary vascular resistance. Recent advances in magnetic resonance imaging (MRI) technology have led to the development of techniques for noninvasive assessment of cardiovascular structure and function, including hemodynamic parameters in the pulmonary circulation, which are superior in their identification of right ventricular morphologic changes. These advantages make cardiac MRI an attractive modality for following up and providing prognoses in patients with PAH. In this review, we summarize recent developments in the use of MRI for the diagnosis, assessment, and ongoing monitoring of patients with PAH. Over the coming decade, it can be anticipated that continued improvements in MRI image acquisition, spatial and temporal resolution, and analytical techniques will result in improved understanding of PAH pathophysiology, diagnosis, and prognostic variables, and will supplement, and may even replace, some of the invasive procedures currently applied routinely to the evaluation of PAH. (J Am Coll Cardiol 2008;52:1683–92) © 2008 by the American College of Cardiology Foundation

Pulmonary arterial hypertension (PAH) is a progressive disorder characterized by abnormally elevated blood pressure of the pulmonary circulation that results, over time, from extensive vascular remodeling and increased pulmonary vascular resistance (PVR). The clinical course of untreated PAH involves relatively rapid progression to right ventricular (RV) failure and death, typically within 3 years of diagnosis (1,2).

Consensus guidelines for screening, detection, and diagnosis of PAH involve a complex series of steps triggered by an initial suspicion that PAH may underlie clinical symptoms, or that PAH may be likely based on family history or risk factors. Transthoracic Doppler echocardiography is the predominant screening modality in early stages of diagnosis, to assess RV structural and functional parameters, including the degree of ventricular remodeling as well as derivation of RV systolic and diastolic pressures and analysis of contraction timing.

Confirmation of PAH diagnosis requires evaluation of hemodynamic parameters via right-heart catheterization (RHC) (which is considered the diagnostic gold standard) including PVR, mean pulmonary artery pressure (mPAP), and the pulmonary capillary wedge pressure. Many parameters derived from RHC, such as cardiac index and right atrial pressure (which reflect changes in RV function), also provide important prognostic information (3–7). When performed in experienced centers, RHC procedures are associated with a low incidence of complications (8); nevertheless, this test is invasive and carries with it a small but real risk of morbidity and mortality, and therefore serial assessments are infrequently performed in the community setting. Moreover, as with other current assessment procedures for PAH, data acquisition requires resting, supine subjects and there is no standard procedure for capturing the hemodynamic changes that occur with upright posture or with activity using RHC. In addition, hemodynamic measurements acquired using RHC are subject to intraindividual spontaneous variability (3,9), most likely because of the challenges faced in the catheterization of patients with PAH, particularly in obtaining accurate wedge pressures. Despite these shortcomings, clinically significant information is gleaned from this study that helps guide therapy. Therefore, noninvasive modalities that can serially assess the changes in RV function may be useful prognostically.

The RV structural and functional assessment plays a central role in both diagnosis and serial follow-up of patients with PAH. However, the geometry of the RV is complex, and it is difficult to evaluate its contractile

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Abbreviations and Acronyms

cMRI = cardiac magnetic resonance imaging
CTEPH = chronic thromboembolic pulmonary arterial hypertension
DCE = delayed contrast enhancement
IPAH = idiopathic pulmonary arterial hypertension
LV = left ventricle/ventricular
mPAP = mean pulmonary artery pressure
MRI = magnetic resonance imaging
PA = pulmonary artery/arterial
PAH = pulmonary arterial hypertension
PVR = pulmonary vascular resistance
RHC = right heart catheterization
RV = right ventricular/ventricle
sPAP = systolic pulmonary artery pressure
VMI = ventricular mass index

motion and functional parameters given the limitations of traditional 2-dimensional echocardiography. Unlike the left ventricle (LV), which can be reasonably modeled as a symmetric ellipsoid, the RV is crescent-shaped in cross section and triangular when viewed laterally. The RV is typically divided into 3 major portions: RV inflow, RV body, and RV outflow. Defining RV systolic function may require assessment of both RV body contractility and motion of the tricuspid annulus (Fig. 1). In comparison with the LV, differences in structure (reduced wall thickness) and in end-diastolic volume (larger in the RV) make the RV more likely to be affected by increased afterload (i.e., pulmonary vascular pressure) than changes in pre-load (10–12).

There are fundamental differences in the physiology of the RV as compared with the LV under normal loading conditions, in part attributable to the coupling of the RV to the low-resistance pulmonic circulation. Changes in pre-load and afterload of RV can cause changes in the geometric shape and wall thickness of the RV (13). This also affects the RV and LV hemodynamics and function. The complex shape of the RV is ideally suited for its physiologic function of pumping blood across the low-resistance pulmonary circulatory system. Because of the unique embryologic/anatomic development of the RV, the contractile pattern of the RV is peristaltic and quite complex (14). As a consequence of the complexity of both the shape and contractile pattern of the RV, routine mathematical models for assessment of RV volumes and function in contrast to LV are extremely difficult and largely inaccurate (15,16). At present, only a true 3-dimensional dataset can be used to accurately assess RV volumes and function.

Pulmonary arterial hypertension affects the right heart and results in right ventricular hypertrophy and dilation and right atrial enlargement (3). The wall thickness of the RV is much less than that in the LV because the RV ejects blood against 25% of the afterload of the LV (17). The RV is thus more compliant than the LV and can accommodate more rapidly to volume overload (18). Gradual increases in afterload, such as occur in PAH, are tolerated because the RV can assemble new sarcomeres in parallel to increase wall thickness. In PAH, the RV undergoes varying degrees of hypertrophy, and, in severe PAH, assumes a spherical shape that has a greater cross-sectional area than the LV, resulting in abnormal septal function that impairs the performance of the LV (17,19). The cardiac remodeling that occurs allows the RV to produce a larger stroke volume to maintain cardiac output. Eventually the enlarged RV's demand for oxygen exceeds the available oxygen supply, and the RV is no longer able to overcome the progressive afterload imposed by PVR. This results in pooling of blood in the RV, which causes chamber dilatation. Valvular regurgitation also occurs in PAH because of incomplete valve closure. These processes can result in contractile dysfunction and in right heart failure.

Recent advances in magnetic resonance imaging (MRI) technology have led to the development of techniques for noninvasive assessment of cardiovascular structure and function, including hemodynamic parameters in the pulmonary circulation, which are superior in their identification of RV morphologic changes (20–22). These advantages make cardiac MRI an attractive modality for following up and providing prognosis in patients with PAH. In this review, we summarize recent developments in the use of MRI for the diagnosis, assessment, and ongoing monitoring of patients with PAH.

Overview of MRI

During the past decade, cardiovascular MRI has been increasingly applied to the evaluation of cardiovascular disease and has become the first-line imaging modality in the assessment of many types of congenital and acquired cardiovascular disorders, including congenital heart disease, myocardial infarction, dilated cardiomyopathy, and large-vessel disease. In addition, cardiovascular MRI is the preferred method for global analysis of ventricular structure/function (e.g., volume, ejection fraction, wall motion abnormalities), myocardial mass, and myocardial viability (21,23). Some of the advantages and disadvantages of MRI are listed in Table 1 (24,25).

The acceptance of cardiovascular MRI has been facilitated by the development of techniques that improve the visualization of blood flow and cardiac parameters such as ventricular volumes, ejection fraction, and myocardial mass. The MRI pulse sequences can be modified so that blood appears darker (black blood turbo spin echocardiography) or lighter (bright blood gradient echocardiographic techniques such as steady-state free precession) than surrounding tissue, which facilitates anatomic studies. These techniques can also be used to generate dynamic (cine) bright-blood MRI images over the duration of a 5- to 18-s breath-hold (which limits respiratory motion artifacts). By combining contiguous bright-blood cine-MRI slices (5 to 10 mm thick) acquired in short-axis orientation, it is possible to calculate end-systolic and -diastolic RV and LV volumes, ejection fractions, and myocardial mass. The high degree of accuracy and reproducibility of these derived measures facilitates the evaluation of disease severity and early-stage

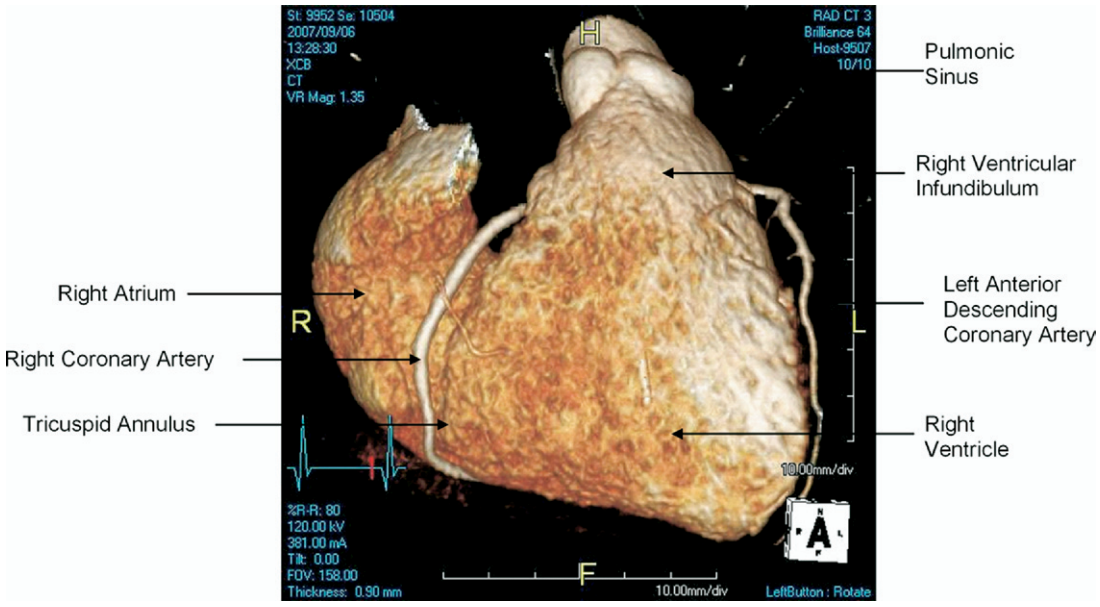

Figure 1 **Surface-Rendered CT Image of the RV**

Surface-rendered CT image of the RV showing a complex RV shape that precludes true assessment of RV structure and function in absence of 3-dimensional dataset. CT = computed tomography; RV = right ventricular/ventricle.

changes in cardiac structure and function, as well as responses to treatment (12,23).

Encoding the MRI signal phase for velocity enables the assessment of flow velocities and volumes passing through blood vessels or cardiac valves. By combining blood velocity with cross-sectional area of the chosen vessel or valve, it is possible to derive stroke volumes, cardiac output, and volumes routed through cardiac shunts. Although this method is analogous to Doppler echocardiography, a key advantage is that MRI analysis of velocity can be conducted in any orientation or plane; in contrast, accurate echocardiographic flow assessment requires the flow to be parallel to the echocardiographic plane (12,23).

Table 1 **Advantages and Disadvantages of Magnetic Resonance Imaging**

Advantages
Unparalleled resolution
Three-dimensional imaging capacity
Noninvasive
Nontoxic contrast agents*
Ability to depict soft tissues
Disadvantages
Long scan times
Artifacts including motion, respiratory, cardiac motion
Incompatibility with pacemakers, defibrillators, and aneurysm clips

*Gadolinium-containing contrast agents are risk factors for the development of nephrogenic fibrosing dermopathy in patients with stage 3 or higher chronic kidney disease, and should be avoided in those with advanced renal failure (24). Reprinted with permission from Lima and Desai (25).

Tissue parameters are best visualized using contrast enhancement techniques (contrast-enhanced MRI), which typically use gadolinium-based magnetic contrast agents. The accumulation of these agents immediately after intravenous infusion is a measure of perfusion and myocardial viability, analogous to the uptake of radioactive technetium in radionuclide perfusion studies. A related technique, delayed contrast enhancement (DCE), reveals areas of fibrosis, necrosis, or edema (12,23).

MRI in PAH Diagnosis and Assessment

Initial studies of cardiovascular MRI showed its ability to distinguish PAH patients from healthy subjects across multiple disease measures. A study using velocity-encoded cine-MRI showed reduced peak systolic velocity and greater post-systolic retrograde flow in the pulmonary arteries of PAH patients; retrograde flow was proportional to pulmonary resistance and inversely proportional to flow volume (26). Another study used multislice–multiphase spin echocardiography and flow-sensitive fast-gradient echocardiography techniques to document RV enlargement and hypertrophy, right atrial enlargement, tricuspid regurgitation, and abnormal motion of the intraventricular septum (27). This study also found a strong correlation between MRI-determined mPAP and end-diastolic RV wall thickness ($r = 0.83$, $p \leq 0.0001$), as well as inferior vena cava diameter ($r = 0.73$, $p \leq 0.0001$). Spin-echo MRI has also documented increased RV mass in idiopathic PAH (IPAH) patients relative to control subjects, with RV mass strongly

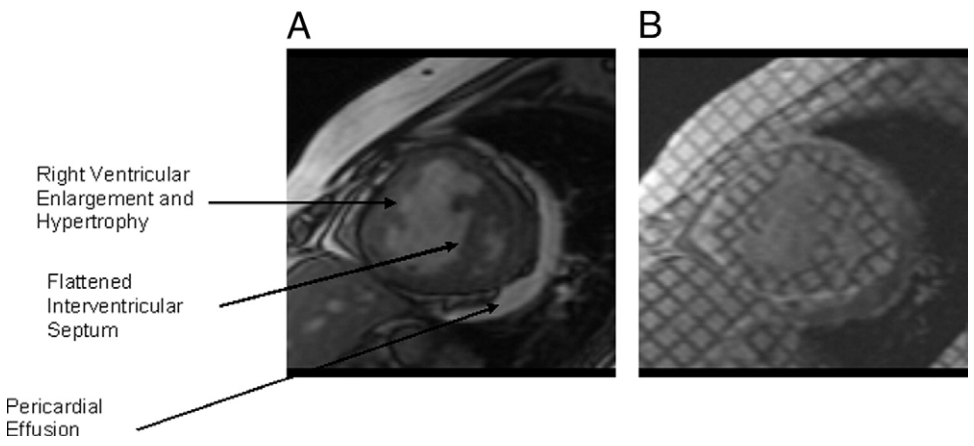

Figure 2 **Short-Axis View of the Heart in a Patient With Pulmonary Hypertension**

(A) End-systolic image (steady-state free-precession magnetic resonance [MR] imaging technique) showing flattened interventricular septum, right ventricular hypertrophy, and pericardial effusion. **(B)** Tagged MR image corresponding to **A**. Tagged MR image is used for analysis of myocardial strain.

correlated with mPAP ($r = 0.75$, $p < 0.003$) (28). Left ventricular septal-to-free wall curvature ratio derived from cardiac MRI produced an accurate and reproducible index for the estimation of RV systolic pressure when compared with a direct measurement from right heart catheterization (29).

Tagged MRI, first described by Zerhouni et al. (30), is a noninvasive technique for measuring 3-dimensional motion and deformation in the heart. Tags are regions of tissue, that is, myocardium, whose longitudinal magnetization has been altered before imaging so that they appear dark in MRI images. These dark areas move with the underlying tissue and act as identifiable landmarks within the heart for the detection of motion (Fig. 2). Using tagged MRI, a study conducted in patients with IPAH showed a significant interventricular asynchrony caused by a longer RV systolic contraction time compared with the LV, presumably a result of a decrease of electrical conductivity over the RV and the large force the RV myocardial fibers must generate to shorten (31). This ventricular asynchrony decreased LV diastolic filling along with septal bowing and decreased RV function, resulting in a decreased LV end-diastolic volume.

Velocity-encoded phase-contrast MRI has been used to study hemodynamic changes associated with PAH. In a recent study of 25 patients with PAH, mean pulmonary artery (PA) peak flow velocity, PA blood flow, and PA distensibility were found to be significantly lower than in a matched group of volunteers ($p = 0.002$, $p = 0.002$, and $p = 0.008$, respectively) (32). This study also documented reduced time to peak PA velocity and steeper velocity increase gradient among PAH patients. Another study compared fast-gradient echocardiographic phase-contrast MRI and radionuclide lung perfusion for assessing differential branch pulmonary blood flow in 12 children with suspected unilateral branch pulmonary artery stenosis (33). The agreement between the 2 methods of calculating total lung blood flow was excellent ($r = 0.98$, $p < 0.0001$).

Contrast-enhancement techniques have revealed important cardiac structural abnormalities among patients with PAH. In one study, zones of DCE were evident in 23 of 25 PAH patients (20). In 7 patients, DCE was confined to the RV insertion points, whereas in the remaining 16 patients, DCE extended from the insertion points into the intraventricular septum. These zones corresponded with areas of mechanical stress (although mechanical stress has not definitively been shown to be the cause), suggesting that elevated RV pressures may lead to tissue abnormalities in these areas. All 16 of the patients in whom DCE was found in the intraventricular septum also showed abnormal septal wall bowing (toward the LV during late RV systole). The DCE was also observed in a study conducted in 15 patients with PAH (34). The extent of the DCE of the myocardium was inversely related to measures of RV systolic function (i.e., RV ejection fraction [$r = -0.63$, $p = 0.001$], RV stroke volume [$r = -0.67$, $p = 0.006$], and RV end-systolic volume index [$r = -0.51$, $p = 0.005$]).

Recently, we showed the utility of defining diastolic function in a similar manner to that of echocardiographic techniques via Doppler techniques (35). Evaluating 34 patients with simultaneous cardiac magnetic resonance imaging (cMRI) and echocardiography, the entire range of diastolic function from grade I through grade IV was evaluated. Using mitral inflow Doppler as the gold standard, cMRI had 100% accuracy to detect the same classification as echocardiography. Additionally, there was 100% sensitivity and 100% specificity to include or exclude the diagnosis of diastolic dysfunction. This finding provided the impetus to evaluate the tricuspid and mitral inflow velocities, showing that in normal patients there was near reproducibility in both the pattern of diastolic function as well as the arith-

metic quantitation of early to late diastolic filling ratios. Specifically, in those with impaired RV function (with and without PAH), there was a clear dichotomization in RV and LV diastolic function, suggesting that cMRI could detect accurately abnormal indexes of RV lusitropy (36). Interestingly, little is written about isolated RV diastolic function using either Doppler flow or tissue Doppler by echocardiography. Early experience via cMRI, using phase velocity mapping, shows that both metrics can be performed for the RV as it can be for the LV.

Given the utility of cardiovascular MRI in identifying structural and functional abnormalities associated with PAH, MRI and RHC are complementary procedures. At this point, the evidence is somewhat contradictory on the utility of cardiovascular MRI to estimate PAP. One study of 26 PAH patients evaluated the calculated ventricular mass index (VMI), the ratio between MRI-derived RV mass and LV mass, as a way to derive PAP (37). The correlation between VMI and mPAP (derived through right-heart catheterization) was stronger than that for echocardiographically derived mPAP; confidence intervals were also narrower for VMI than for echocardiography. The sensitivity and specificity of VMI as a predictor of mPAP (using VMI >0.6 as a diagnostic cutoff) were 84% and 71%, compared with 89% and 57% for echocardiography.

Laffon et al. (22) developed a computerized algorithm for estimating mPAP based on an MRI assessment of physical parameters (e.g., pulmonary artery cross-sectional area, blood flow velocity) that is weighted using patient-specific biophysical parameters (e.g., height, weight, heart rate). When this algorithm was applied to a series of 31 patients undergoing RHC, the calculated mPAP based on MRI-derived parameters correlated strongly with catheterization-derived values ($r = 0.92$).

In another study, 29 patients with IPAH or chronic thromboembolic pulmonary arterial hypertension (CTEPH) were evaluated with fast-perfusion MRI and high-resolution MRI angiography, performed using parallel acquisition techniques (38). Both of the MRI-based techniques were compared and showed good agreement with radiation-based alternatives (fast-perfusion MRI with radionuclide perfusion scintigraphy; MRI angiography with digital subtraction angiography and contrast-enhanced computerized tomography). The combination MRI assessment resulted in correct diagnoses for 26 patients (90%).

In contrast to these generally positive results, Roeleveld et al. (39) assessed 44 patients with established PAH and found poor correlation between catheterization-derived mPAP and 5 different MRI-derived measures, including pulmonary vascular index, acceleration time (defined as time from onset of PA forward flow to maximum velocity), the ratio between acceleration time and ejection time, and the Laffon algorithm discussed previously. The only significant correlation between catheterization-based mPAP and MRI-based measures was for VMI ($r = 0.56$, $p < 0.001$). However, using a VMI cutoff of >0.6 to define PAH [as suggested by Saba et al. (37)] would result in a missed diagnosis in 9 patients, a false-negative rate of 20%. The investigators conclude that at this time MRI-derived measures may be reasonable for use in screening and differential diagnosis; however, they are not yet capable of replacing right-heart catheterization in confirming PAH diagnosis.

Finally, a recent study examined 59 patients with PAH with both RHC and phase-contrast MRI (40). The parameters determined from MRI were PA areas, PA strain, average velocity, peak velocity, acceleration time, and ejection time. These parameters were then compared with those measured from RHC, that is, mPAP, systolic PAP (sPAP), and pulmonary vascular resistance index (PVRI). It was reported that average velocity had the best correlation with mPAP, sPAP, and PVRI ($r = -0.86$, $p < 0.001$). This strong correlation between average blood velocity and pulmonary pressures and resistance might allow noninvasive diagnosis of PAH.

MRI-Guided Catheterization

Noninvasive MRI alone does not yet seem to be able to fully assess RV pump parameters, in part because it has limited ability to assess load-independent parameters of function (such as myocardial contractility) in patients with chronically pressure overloaded RVs. A novel hybrid technique, real-time MRI-guided catheterization (41), has recently been applied to PAH assessment. Kuehne et al. (42) initially showed the ability of MRI-guided catheterization to construct RV pressure-volume loops, and in turn to calculate RV afterload, myocardial contractility, pump function, and RV-pulmonary artery coupling in healthy volunteers and PAH patients. Despite significantly greater myocardial contractility among PAH patients, RV pump function was compromised compared with healthy volunteers, in part because of inefficient coupling between the RV and pulmonary circulation.

In addition to mPAP, accurate real-time estimation of PVR is critical in PAH workup, because PVR assessment can provide a picture of vascular remodeling as well as response of the pulmonary vasculature to various pharmacological agents. In a second study, Kuehne et al. (43) showed that PVR assessment using MRI-guided catheterization and MRI velocity mapping provided more reproducible results than the traditional thermodilution method. In addition, this technique seems to provide the ability to sample PVR more comprehensively (including both overall and branch-specific resistance) than can be achieved using Doppler guidewires.

Although MRI-guided catheterization remains an invasive technique, it avoids the minimal risk of radiation exposure associated with traditional RHC and may be more appropriate for serial assessment over time (especially in pediatric patients).

MRI in PAH Treatment Selection and Monitoring

In addition to PAH diagnosis, right-heart catheterization is the currently preferred modality for assessing acute vasoreactivity in PAH patients to help determine initial treatment selection. Vasodilator response may also provide prognostic information with regard to the extent of vascular remodeling and retained cardiac function (44,45). The MRI-based techniques may be closer to replacing RHC for treatment selection and monitoring than with regard to diagnosis. A pilot study in 19 IPAH patients shortly after right-heart catheterization showed that MRI assessment of main pulmonary artery distensibility was highly correlated with vasodilator response ($p = 0.01$) (45). A cutoff value of 10% distensibility enabled responders to be distinguished from nonresponders with 100% sensitivity and 56% specificity.

The MRI may find its most immediate applicability in PAH management in serial monitoring to determine treatment response. One study used cine MRI and MRI velocity coding to assess response to continuous intravenous epoprostenol in 11 IPAH patients over 1 year (46). The MRI analysis showed a significant increase in RV stroke volume (from 34 ± 11 ml to 41 ± 11 ml; $p < 0.05$) and a 12.5% reduction in total PVR ($p = 0.06$). Although RV mass and mPAP remained relatively unchanged, there was no evidence of deterioration. The MRI analysis showed that the most significant improvement in RV stroke volume was observed during the first 4 months of treatment. Furthermore, there was a close relationship between RV stroke volume improvement and increase in 6-min walk distance, the standard measure of functional improvement in IPAH. The latter observation is especially important because it has been difficult to date to correlate functional improvement with improvement in hemodynamic parameters in PAH clinical studies.

Cardiac MRI has been used in combination with tissue Doppler echocardiography to show improvements in myocardial perfusion (using MRI) and ventricular contractility (using tissue Doppler echocardiography) in patients with systemic sclerosis who were treated with bosentan (47). In 18 patients, 4 weeks of treatment with bosentan increased both myocardial perfusion (as evaluated by MRI) and myocardial function (as evaluated by tissue Doppler echocardiography).

Finally, MRI has been used to show restoration of the RV after pulmonary endarterectomy in patients with CTEPH (48). Before surgery, there were significant differences between patients with CTEPH and healthy controls in right ventricular volumes, LV end-diastolic volume, RV mass, and leftward ventricular septal bowing. After at least 4 months post-surgery, pulmonary hemodynamics improved in the 17 patients, and normalization occurred in the following measures: RV and LV volumes and leftward ventricular septal bowing. Thus, MRI was able to evaluate cardiac remodeling in CTEPH patients and to show restoration of the RV after pulmonary endarterectomy.

Cardiovascular MRI in PAH: Strengths and Weaknesses

The value of cardiovascular MRI in the management of PAH is most appropriately evaluated in comparison with the 2 principal technologies that generate structural and functional parameters similar to those provided by MRI, namely RHC and echocardiography. At the current time, MRI-based assessment does not yet seem ready to replace RHC with respect to confirmation of PAH diagnosis; however, the hybrid technique of MRI-guided catheterization may facilitate comparable diagnostic clarity while reducing radiation exposure. An MRI provides a far more complete picture of overall RV structure and function than RHC, and can also provide extremely useful information with regard to PA pressure and blood flow. Preliminary results suggest that for ongoing assessment of treatment response, MRI may already be superior to invasive methods, with the potential to more tightly align functional and hemodynamic response measurements in future studies of PAH treatment.

Provocative pharmacologic stress testing using cMRI has been shown to be advantageous and clearly has been shown to offer a capability far above that of echocardiography (49,50). The explanation for this finding is that, as described earlier, the fidelity of cMRI offers as much or more for the RV as it does for the LV. Although little has been written about such stress testing for the PAH patient, it is conceivable that even greater accuracy of wall motion abnormalities would be detectable if such were even considered for the PAH patient by echocardiography. Further, the response to increased afterload/inotropy when incorporated with volumetrics and contractile function would be paramount in the evaluation of RV performance in patients with PAH, especially in the interrogation of response to therapy or when determining the end of pharmacologic therapeutic options in anticipation of RV assist device or lung transplantation considerations.

Echocardiography plays an important role in the screening and diagnosis of PAH and, despite limitations imposed by 2-dimensional imaging, provides reasonable estimates of PA pressures, as well as ongoing assessment of changes in RV structure and function. Echocardiography has also proved valuable in the evaluation of structural and functional responses to treatment. Because of its widespread availability (relative to MRI), echocardiographic techniques are likely to retain a prominent position in PAH screening, diagnosis, and management (51,52).

In addition, new echocardiographic techniques with potential utility in PAH continue to be introduced. Two-dimensional strain echocardiography, a novel method for the assessment of regional contractility, has recently been combined with tissue Doppler echocardiography to docu-

Table 2 Parameters of Pulmonary Hypertension by Noninvasive Imaging Method

Parameter	Noninvasive Imaging Method of Choice	Optimal View or Imaging Window
Anatomy		
Pulmonary artery size	cMRI	High axial image
Qualitative RV size, hypertrophy, trabeculations	Echocardiography	Apical 4-chamber, parasternal long-axis 4-chamber, short-axis series for volumes, function, and masses
Quantitative RV size, mass, trabecular mass	cMRI	
Function		
RV free wall motion	cMRI	4-chamber, short-axis
Interventricular septal motion	cMRI or echocardiography	4-chamber, short-axis
Qualitative systolic function	Echocardiography	4-chamber, parasternal short-axis
Quantitative systolic function	cMRI	Short-axis series
Diastolic function	Echocardiography	AV valve inflow parameters, tissue Doppler
Hemodynamics		
Pulmonic valve motion	Echocardiography	High SA M-mode
RVOT flow	Echocardiography	High SA pulse-wave Doppler
Pulmonary artery pressure	Echocardiography	TR, PR velocities, any flow into right heart

Reproduced with permission (56).

AV = atrioventricular; cMRI = cardiac magnetic resonance imaging; PR = pulmonic regurgitation; RV = right ventricle; RVOT = right ventricular outflow tract; SA = sinoatrial; TR = tricuspid regurgitation.

ment RV dysfunction in patients with PAH, as well as improvements after vasodilator therapy (53). Although it has been used to date in relatively limited clinical settings pertaining to PAH (primarily in patients with CTEPH), 3-dimensional echocardiography may ultimately provide functional and structure information comparable with MRI (54,55).

The introduction in recent years of more effective PAH interventions makes it likely that various combinations of MRI and echocardiographic assessment techniques will be

Table 3 A Comparison of the Usefulness of the Different Imaging Modalities and RHC for Characterizing Different Parameters*

Parameter	Modality		
	Cardiac MRI	Echocardiography (Including 3-Dimensional Echocardiography)	RHC (Including Right-Sided Angiocardiography)
RV assessment			
Volumes	+++	++	+
Ejection fraction	+++	++	+
Strain	+++	++	−
RV pressure	−/+	++	+++
Stroke volume	+++	+	+++
Mass	++	−/+	−
RV remodeling including septal curvature	+++	++	−
Tricuspid regurgitation	++	+++	+
Miscellaneous (pericardial effusion, pulmonary embolism, and other incidental findings)	++	+	+
RA assessment	++	+	−
RA pressure	−	−	+++
PA dimensions	+++	+	+
PA distensiblity	+++	+	−/+
PA hemodynamics	−/+	+	+++
Quantitative lung flow	+++	−	−

*Ideally invasive MRI (i.e., simultaneous evaluation of MRI-derived volume and flow parameters with RHC derived pressure measurements) may be the most accurate method of assessing cardiac hemodynamics.

− = not useful; + = may be useful; ++ = useful; +++ = extremely useful; MRI = magnetic resonance imaging; PA = pulmonary artery; RA = right atria; RHC = right heart catheterization; RV = right ventricle.

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Table 4 Current Issues in Cardiovascular Magnetic Resonance Imaging

Large number of technical parameters that the scanner operator needs to know
Large number of parameter choices results in different imaging sites using protocols with different parameters, making a comparison of images difficult
Intensive training is required for scanner operators
Lack of a standardized viewing and reporting format
Imaging centers have to create their own viewing tools
Viewing takes so much time that it limits patient throughput
Lack of a standardized nomenclature for magnetic resonance sequences and parameters
Vendors choose different names for the same or similar techniques to differentiate them from their competitors
Focus on research
Small number of current procedural terminology codes, each with limited scope
Current procedural terminology codes have not kept up with technological developments

applied to PAH diagnosis and management in the near future. These combinations provide perhaps the best hope for near-term replacement of invasive RHC. Moreover, as suggested by the relatively recent development of MRI-based techniques for right-heart evaluation discussed here, rapid advancement in these techniques is to be expected. Continuing improvements in MRI spatial and temporal resolution, as well as in algorithms for post-acquisition data analysis, make it likely that cardiovascular MRI (alone and in combination with echocardiography) will largely supplant invasive techniques in the future. A comparison of the utility of cardiovascular MRI versus echocardiography for measuring different parameters important in PAH is shown in Table 2 (56). Table 3 shows a comparison of the utility of different imaging modalities and RHC for providing information about various cardiac parameters.

Certain contraindications remain for MRI that may prevent its universal use in all PAH patients; these include neurostimulators, cochlear implants, pacemakers, and other implanted devices, as well as patient claustrophobia. However, at least some of these are considered relative rather than absolute contraindications. Some studies have shown that cardiovascular MRI may be feasible in patients with implanted pacemakers (57,58), although widespread routine use of MRI in these patients requires additional study.

At the present time, there are important issues that hinder the widespread adoption of cardiovascular MRI for routine clinical use (Table 4) (59). The complex user interface for the instrument requires considerable operator training. The lack of standardized protocols and viewing formats puts a burden on each imaging center to develop their own. Finally, the focus toward using cardiovascular MRI for research means that billing codes for procedures are suboptimal and have not kept up with technological advances.

Future Directions

It has become apparent that the availability of new effective PAH therapies not only is contributing to revised concepts in PAH management, but also has heightened the need for reliable, preferably noninvasive, methods for monitoring disease course and treatment response. The information derived from these methods will certainly change clinical practice, and, equally important, will help fill in some of the existing knowledge gaps pertaining to PAH pathophysiology, prognostic factors, subclassifications, and relationships between hemodynamic parameters and exercise function, quality of life, and clinical management.

Some research directions suggested by the studies described here include expanded use of DCE to evaluate fibrosis and other tissue changes, evaluation of LV/RV interdependence and coupling, better understanding of RV-PA coupling, and the relationship between hemodynamic parameters and changes in lung perfusion. Enhancement of current knowledge in these areas, in turn, can be expected to improve the design of clinical studies and lead to further refinements in the management of PAH.

Conclusions

Over the past 2 decades, improvements in MRI spatial and temporal resolution and in post-acquisition analytic algorithms have led to the increased incorporation of MRI as a key element in numerous aspects of cardiovascular assessment and treatment. In assessing how this highly dynamic, rapidly evolving family of technologies has impacted recognition and management of PAH, it is clear that cardiovascular MRI is now regarded as the reference standard in the assessment of RV structure and function, that is, via the measurement of RV volumes and ejection fractions, and is likely to supplant invasive and/or radiation-based techniques for evaluating myocardial function. Over the coming decade, it can be anticipated that continued improvements in MRI image acquisition, spatial and temporal resolution, and analytical techniques will result in improved understanding of PAH pathophysiology, diagnosis, and prognostic variables, as well as the replacement of most if not all invasive procedures currently applied routinely to the evaluation of PAH.

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