MRI Catheterization in Cardiopulmonary Disease

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Diagnosis and prognostication in patients with complex cardiopulmonary disease can be a clinical challenge. A new procedure, MRI catheterization, involves invasive right-sided heart catheterization performed inside the MRI scanner using MRI instead of traditional radiographic fluoroscopic guidance. MRI catheterization combines simultaneous invasive hemodynamic and MRI functional assessment in a single radiation-free procedure. By combining both modalities, the many individual limitations of invasive catheterization and noninvasive imaging can be overcome, and additional clinical questions can be addressed. Today, MRI catheterization is a clinical reality in specialist centers in the United States and Europe. Advances in medical device design for the MRI environment will enable not only diagnostic but also interventional MRI procedures to be performed within the next few years.

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Catheterization plays a central role in the diagnostic evaluation of patients with intracardiac shunts, complex congenital heart disease, pulmonary vascular disease, cardiomyopathy, cor pulmonale, and heart failure. Elevated pulmonary arterial pressure is a hemodynamic finding common to all these disease processes. Establishing the cause of pulmonary hypertension requires complex diagnostic algorithms involving numerous noninvasive and invasive tests. Today, catheterization remains the best available investigative tool for confirming diagnosis, quantifying severity of disease, and determining treatment. Guidelines^{1–3} recommend catheterization be performed in all patients

with symptoms and echocardiographic suspicion of pulmonary hypertension or prior to initiation of therapy.

Hemodynamic parameters shown to be associated with an increased risk of death include increased mean pulmonary artery pressure, increased mean right atrial pressure, and decreased cardiac index.⁴ Most guidelines define pulmonary hypertension based on elevated mean pulmonary artery pressure alone. However, with disease progression, mean pulmonary artery pressure may actually fall as the right ventricle fails. For this reason, pulmonary vascular resistance is a more compelling standard for the diagnosis of pulmonary hypertension because it takes into account both pressure and flow. Resistance measurement has not entered guideline care because accurate measurement of pulmonary flow is not possible in the presence of tricuspid regurgitation, typical in these patients, using conventional thermodilution techniques. It is important to consider that the cause of elevated pulmonary pressure is not always pulmonary vascular pathology. For example, in patients with high transpulmonary flow, such as in pregnant women or in patients with anemia, sepsis, thyrotoxicosis, or intracardiac shunt, pulmonary pressure can be elevated in the presence of normal pulmonary vascular resistance. Provocative testing with vasodilators, such as inhaled nitric oxide plus 100% oxygen, is recommended because vasoreactivity predicts responsiveness to prostacyclin analogs, endothelin-receptor antagonists, or phosphodiesterase

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type 5 inhibitors and also identifies those patients with a better prognosis.

LIMITATIONS OF CATHETERIZATION

Catheterization techniques for measurement of cardiac output (necessary for the quantification of pulmonary vascular resistance) are subject to error. The thermodilution technique is inaccurate in patients with low flow states, intracardiac shunts, or significant valvular regurgitation (eg, tricuspid regurgitation).⁵ Thermodilution should, therefore, be avoided in patients with pulmonary hypertension who often have significant tricuspid regurgitation. The Fick technique is inaccurate in conditions in which venous and arterial hemoglobin saturation values approach each other (eg, with large intracardiac shunts or during vasoreactivity testing with nitric oxide and 100% oxygen). The Fick principle incorporates total body oxygen consumption, but measuring oxygen consumption is labor intensive. Instead, most laboratories estimate oxygen consumption using assumptions such as LaFarge and Miettinen,⁶ based on body surface area, age, and heart rate. If the Fick principle is used, this estimate can introduce significant error into cardiac output calculations.

LIMITATIONS OF NONINVASIVE EVALUATION

Echocardiography is typically the first test performed in patients with suspected pulmonary hypertension. The established method for estimating pulmonary artery pressure with echocardiography involves measuring the maximal velocity of tricuspid regurgitation.⁷ Alternative markers of pulmonary hypertension, including pulmonary artery acceleration time,⁸ flattening of the interventricular septum, and pulmonary regurgitant velocity, have been proposed in the absence of tricuspid regurgitation.⁹ Calculating pulmonary vascular resistance is not possible because echocardiography cannot accurately measure left atrial pressure and arguably cannot accurately measure transpulmonic flow and because errors are common in measuring the Doppler envelope of the tricuspid regurgitation jet. Evaluating the right ventricle with echocardiography is difficult because of its complex geometry¹⁰ and its anatomic position beneath the sternum, exaggerated in those most affected.¹¹ Echocardiography is further limited by poor acoustic windows in patients with large body habitus or with advanced lung disease (eg, COPD).

Cardiac MRI is the best available imaging modality for structural and functional assessment of the right ventricle.¹² Right ventricular dysfunction is a determinant of functional capacity and prognosis in pulmonary

artery hypertension,¹³ chronic heart failure,¹⁴ myocardial infarction, and mitral regurgitation.¹⁵ Whereas pulmonary artery pressure does not strongly correlate with symptoms or survival, right ventricular stroke volume and end diastolic dimensions by MRI are independent predictors of mortality in patients with primary pulmonary hypertension.¹⁶ The 6-min walk test of functional capacity, used as the primary end point in most pulmonary hypertension pharmaceutical trials,¹⁷ correlates better with right ventricular function than with pulmonary artery pressure. Pulmonary arterial stiffness, measured with MRI by relative cross-sectional area in systole and diastole, also predicts mortality in patients with pulmonary hypertension.¹⁸ In patients with chronic heart failure, right ventricular function correlates better with exercise capacity than does left ventricular function,¹⁹ and elevated pulmonary artery pressure and right ventricular dysfunction have been shown to be independent predictors of mortality.¹⁴ Therefore, it is critical to combine hemodynamic variables with a functional evaluation of the right ventricle and the pulmonary vasculature.

MRI CATHETERIZATION OFFERS ADDITIVE DIAGNOSTIC VALUE COMPARED WITH STAND-ALONE MRI OR CONVENTIONAL CATHETERIZATION

MRI catheterization addresses all the previously mentioned limitations by simultaneously measuring the pressures, flows, and volumes of the desired cardiac chambers. Volumetric analysis of cardiac function (such as end-diastolic and end-systolic volumes) or MRI (velocity-encoded, also known as phase-contrast) flow techniques can measure stroke volume and pulmonary or systemic cardiac output. In addition, intracardiac shunts (Qp:Qs) can be identified from mismatched pulmonary artery and aortic flows. Hybrid parameters, such as pulmonary vascular resistance or pulmonary artery compliance, can be derived from assimilation of MRI measurements and catheterization pressures.

Although pulmonary vascular resistance can be measured accurately at rest using conventional Fick oximetric techniques, provoked pulmonary vascular resistance measurements during administration of inhaled oxygen and nitric oxide are inaccurate. Muthurangu and colleagues²⁰ elegantly demonstrated this discordance in 2004 using invasive pressure and cardiac output derived from phase-contrast MRI at baseline and during nitric oxide plus 100% oxygen vasoreactivity testing. Although unproven, similar inaccuracy can be expected during other stress-provoked measures of pulmonary vascular resistance.

Other parameters such as pulmonary artery compliance can be derived only from a combined approach.²¹

In 2004, Kuehne and colleagues²² demonstrated it was possible using MRI catheterization to infer right ventricular pressure-volume relationships in single-beat measurements, to estimate right ventricular contractility, pulmonary arterial elastance, and ventricular-arterial impedance mismatch.

MR angiography, with or without contrast, provides detailed insight into structural heart abnormalities. Moreover, characterization of myocardial tissue is possible using T2 assessment of myocardial edema, infiltration, and inflammation²³; T1 assessment of myocardial extracellular volume and collagen content for fibrosis^{24,25}; and early and late gadolinium enhancement of acute and chronic myocardial infarction.²⁶ More elaborate time-resolved imaging of flow (“four-dimensional flow”) may be helpful in select cases of complex congenital and postsurgical anatomy, but often at the expense of intolerably prolonged procedures.^{27,28}

MRI CATHETERIZATION IS A CLINICAL REALITY TODAY

MRI catheterization is typically performed in a combined MRI and radiographic cardiac catheter laboratory (Fig 1). To enable interventional MRI procedures, the MRI room must be equipped with display monitors or projectors so the operator can view images and patient hemodynamic parameters/waveforms. MRI generates acoustic noise, so specialized sound-suppression headsets are required to allow the operator, patient, catheterization laboratory staff, and MRI technician to communicate while scanning. It can be performed in patients who are awake or under general anesthesia, and it can be performed in patients in the ICU, just as is conventional MRI, using suitable patient care equipment. Most MRI studies can now be performed “free breathing,” negating the need for the patient to perform multiple breath holds. Newer MRI hardware allows real-time MRI at greater than 10 frames/s, which is sufficient for safe navigation of catheters within the intravascular space. The unique ability of MRI to “slice” through any plane enables the operator to visualize the relative position of vascular structures and their connections (Fig 2). Commercially available balloon-tip catheters filled with either air or gadolinium contrast are visualized readily (Fig 3).

Razavi and colleagues²⁹ first reported diagnostic radiograph/MRI-guided right-sided heart catheterization in 2003. We recently reported our experience of stand-alone diagnostic MRI catheterization in adults at the National Institutes of Health.³⁰ Sixteen patients underwent paired radiograph and MRI-guided catheterization for comparison. Total catheterization time and individual procedure steps required approximately the same amount of time, irrespective of image guid-

ance modality. To date, we have performed almost 50 such procedures using only MRI guidance and, indeed, have reclassified MRI catheterization as a standard clinical procedure in our institution. Outside the United States, MRI catheterization is performed in two pediatric hospitals in London, England (Evelina Children’s and Great Ormond Street Hospitals). As of March 2013, the worldwide published and unpublished (V. Muthurangu, MD, and R. Razavi, MD, oral communication, 2013) cardiac MRI catheterization experience totals > 450 subjects.

FURTHER ADVANTAGES OF MRI CATHETERIZATION

In the pediatric population, both MRI and catheterization usually require sedation or general anesthesia. Combining them into a single procedure reduces the sedation requirement and associated risk to the patient, as well as the overall cost. Delineation of abnormal anatomy under fluoroscopic guidance requires iodinated contrast injections, particularly in children with complex corrected or noncorrected congenital heart disease, whereas MRI offers unrivalled anatomic imaging without the need for contrast agents.^{31,32} In adults with congenital heart disease, MRI is the recommended technique for diagnosis and management.³³

Both physicians and patients are increasingly mindful of medical radiation. In the pediatric population, young patients with complex congenital heart disease often require serial catheterization. There is evidence that chromosomal changes may result from medical radiation exposure.^{34,35} Radiation-free catheterization is an opportunity to reduce the cumulative radiation dose. Even in the adult population, there is a growing body of evidence regarding the potential harm from medical radiation.³⁶ An important diagnosis to consider in all patients with pulmonary hypertension is chronic thromboembolic disease. Most patients undergo a non-invasive screening test, usually ventilation-perfusion scintigraphy or CT pulmonary angiography. Although not yet adopted widely, MRI offers a radiation-free alternative. Gadolinium-enhanced MRI lung perfusion sequences (Fig 4) can be added easily to an MRI catheterization protocol.³⁷

ADDED VALUE OF PHYSIOLOGIC PROVOCATION

The value of catheterization is enhanced when the assessment of pressures and right ventricular function are compared among different physiologic conditions. Many patients with cardiopulmonary disease, including those with elevated pulmonary artery pressure, are asymptomatic at rest and only develop symptoms with exercise. Yet we perform most of our evaluation

FIGURE 1. The combined MRI and radiograph cardiac catheter laboratory at the National Institutes of Health. A, Biplane radiograph system. B, The patient, who remains on a single table throughout, is transferred between systems. C, View from radiograph system into MRI room. The cardiac defibrillator must be kept outside the MRI room. D, MRI catheterization with real-time MRI images displayed to the operator inside the room. Note that operators, staff, and patients wear sound-suppression headsets.

(both invasive and noninvasive) at rest. Provocative testing with exercise or IV fluid volume can be useful to unmask latent symptoms and pathologic findings.³⁸ For example, in patients with nonsystolic left ventricular dysfunction (also known as diastolic dysfunction or heart failure with preserved ejection fraction), pulmonary capillary wedge pressure (or left ventricular end-diastolic pressure) and pulmonary artery pressure are often normal at rest but rise with exercise³⁹ or volume⁴⁰ challenges. In patients with pulmonary hypertension, a lack of right ventricular functional augmentation and pulmonary vascular resistance reduction

with exercise predict poor prognosis.⁴¹ In patients with pulmonary hypertension due to left ventricular diastolic dysfunction and pulmonary venous congestion, a lack of reduction in left ventricular end-diastolic pressure to afterload reduction (eg, with sodium nitroprusside infusion) suggests a severe irreversible restrictive myocardial process. MRI during hemodynamic provocation should reveal functional and morphologic perturbations not necessarily evident on pressure tracings (eg, lack of right ventricular functional augmentation with exercise in patients with pulmonary hypertension).

FIGURE 2. MRI provides structural information for diagnosis and catheter navigation. A, Four-chamber image showing severely dilated RV relative to LV. B, Real-time image showing anomalous pulmonary vein draining into the superior vena cava (SVC) (arrow). LV = left ventricle; RV = right ventricle.

FROM DIAGNOSTIC TO INTERVENTIONAL MRI CATHETERIZATION

Current MRI techniques for needle, catheter, or device visualization rely on creating an imaging artifact (eg, with ferrous material) or using contrast agents (eg, air or gadolinium-filled balloons). This strategy has limitations because it requires the device to be confined within the selected imaging slice, and in the case of balloon-tip catheters, the shaft of the device remains invisible. To improve visualization of the whole device, “active” MRI catheters can be specifically engineered to contain antenna elements,⁴²⁻⁴⁴ which permits enhanced visualization, for example, by depicting the device in color during anatomic images, or by

FIGURE 3. MRI catheterization real-time images with gadolinium-filled balloon-tip (arrows) catheter. A, Inferior vena cava. B, SVC. C, RV. D, Right pulmonary artery. See Figure 2 legend for expansion of abbreviations.

allowing the device to be visualized even when it lies outside the selected imaging slice.

Whole-device visualization also enables more complex interventional procedures to be performed under MRI guidance. At the National Institutes of Health, we have performed numerous preclinical MRI-guided interventional procedures using active devices, including recanalization of chronically occluded peripheral arteries, targeted myocardial cell delivery, percuta-

neous transthoracic left ventricular access for delivery of large devices,⁴⁵ direct transthoracic ventricular septal defect closure,⁴⁶ atrial septal puncture and balloon septostomy,⁴⁷ aortic coarctation stenting,⁴⁸ and MRI-guided pericardiocentesis.⁴⁹

The great advantage of MRI over radiographic fluoroscopy is the ability to view the interaction of devices with the surrounding tissue in real time. For example, while deploying stents or stent grafts or cardiac implants, the operator can watch for and address iatrogenic rupture, dissection, or pericardial tamponade. Identifying complications early should reduce the risk of these high-risk interventions.

Specifically, MRI-safe catheter devices for use in humans are currently in development or awaiting regulatory approval. We predict that the next few years will see interventional MRI catheterization become a more widespread clinical reality.

CONCLUSIONS

The diagnosis of complex cardiopulmonary disease requires the integration of structural, functional, and

FIGURE 4. Gadolinium-enhanced MRI first-pass lung perfusion images. A, A patient with normal pulmonary pressure. B, A patient with chronic thromboembolic pulmonary hypertension. Arrows indicate multiple segmental and subsegmental perfusion defects.

hemodynamic parameters from a combination of non-invasive and invasive investigations. MRI catheterization addresses all these considerations in one single study and provides more information than either modality alone. This reduces the burden of medical investigations on the patient, simplifies the interpretation of multiple tests for the physician, and may reduce the overall cost. In the future, interventional MRI catheterization will allow radiation-free therapy with a superior device and tissue visualization compared with existing imaging guidance techniques.

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