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EDITORIAL COMMENT

Differentiation of Cardiac Masses by CMR

Judging a Character by the Company It Keeps*

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Noninvasive cardiac imaging specialists are the detectives of the cardiology world. Using different modalities and techniques, we are able to piece together clues and use circumstantial evidence to deduce the likely culprit. Like all investigators, we are subject to our own intrinsic biases; however, the prejudice of experience may be our most valuable quality. When it comes to assessment of cardiac masses, accurate diagnosis relies on pattern recognition and "guilt by association." In the criminal world, suspects are often judged by the company they keep, and our typical method of cardiac mass differentiation is no different. However, suspicions must be proven beyond reasonable doubt. Cardiac magnetic resonance (CMR) is well positioned to provide more objective evidence to support our clinical suspicions and help close the case.

Just like with criminals, there are grades of danger among cardiac masses. Our first role is to determine if it is something we need to be concerned about and act upon immediately. Can it be observed over time, or can it be ignored and quickly forgotten? The fundamental principle is to determine whether a mass is benign or malignant. Large masses with features of invasion or irregular margins are obviously the most concerning. Other suspicious characteristics include: broad-based attachment, loss of tissue planes, traversing of cardiac chambers, tissue heterogeneity with surrounding enhancement, and extracardiac abnormalities that may represent primary disease or metastatic spread. Typically, these features reflect malignant disease and have a much poorer prognosis. Treatment might be targeted at relief of symptomatic obstruction because resection with curative intent is typically not feasible. If a mass is suspected of being malignant, autopsy studies highlight that secondary malignancy, as opposed to a primary cardiac tumor, is 20 to 40 times more common (1). Location can also help determine the cause of the tumor, whether it is a direct invasion from breast or lung malignancies, venous extension from a renal cell carcinoma, hematological seeding from remote primary malignancies, or aggressive mediastinal tumors. In contrast, primary intracardiac tumors are more likely to be benign (2) and therefore have a better prognosis. In these situations, intervention is reserved for relief of obstruction or if there are associated issues such as embolization or thrombus formation. In the majority of cases, complete resection is possible and remedial.

Intracardiac thrombi are typically diagnosed by the "company they keep." A left atrial mass in the setting of mitral stenosis or atrial fibrillation is a thrombus until proven otherwise. Left ventricular masses associated with apical aneurysms or other regional wall motion abnormalities are highly suggestive of mural thrombi. In this setting, anticoagulation and watchful waiting may be a reasonable management strategy; however, once the milieu for thrombus development has been proven, lifelong anticoagulation is usually warranted in those without risk of bleeding. Lastly, although vegetations may be difficult to differentiate from thrombi, clinical correlation should provide some clues to etiology.

The principles outlined here can be applied to any modality of cardiac imaging for initial cardiac mass assessment. However, the adoption of CMR into our imaging repertoire has enabled further differentiation of cardiac masses on the basis of multiplanar imaging and tissue characterization. Different CMR sequences exploit specific mass characteristics, which are largely determined by their vascularity, their solid or cystic nature, and associated structures. Noncontrast T1- and T2-weighted turbo spin echo and cine imaging allow assessment of mass size, location, mobility, surrounding structures, and dynamic information

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TABLE 1 Stratification of Cardiac Masses on The Basis of Typical CMR Characteristics

	Thrombus	Benign Tumor	Malignant Tumor
Structural and functional assessment: gradient echo cine imaging			
Size	Small	Small, usually well circumscribed	Large, irregular margins
Uniformity of tissue signal	Homogeneous	Homogeneous or heterogeneous (due to regions of necrosis)	Heterogeneous
Mobile	Yes	Yes	No
Surrounding structures and location	Associated with left ventricular dysfunction, regional wall motion abnormalities, venous catheters, left atrial appendage, or mitral stenosis	Usually well circumscribed, can cause mass effect, often located in a typical position such as the left atrium or interatrial septum	Invasion of surrounding structures without adherence to tissue planes, unusual locations and involving multiple cardiac chambers, extracardiac disease (including lung or breast masses)
Other	Reduces in size after anticoagulation		Associated features such as pericardial/pleural effusions
Tissue characterization			
T1-weighted turbo spin echo sequence	Hyperintense	Variable intensity - Lipomas = hyperintense - Cysts = hypointense	Variable intensity
T2-weighted turbo spin echo sequence	Isointense/hypointense (old thrombus)	Isointense/hyperintense	Isointense/hyperintense
T2 STIR-weighted sequence	Isointense/hypointense (old thrombus)	Isointense/hyperintense (cystic lesions and hemangiomas)	Isointense/hyperintense (osteosarcomas, angiosarcomas, and leiomyosarcomas)
Fat saturation sequence	Isointense	Isointense/hypointense (lipomas)	Isointense/hypointense (liposarcomas)
First-pass perfusion (saturation-recovery fast gradient-echo sequence)	No	Yes	Yes
T1 Look-Locker sequence (post-contrast)	Hypointense with longer T1 time	Hyperintense with shorter T1 time (longer T1 time if cystic)	Hyperintense with shorter T1 time
Delayed gadolinium enhancement	No (may have enhancement of adjacent myocardial scar)	Yes (especially hemangiomas, fibromas and rhabdomyomas)	Yes (especially angiosarcomas)

CMR = cardiac magnetic resonance; STIR = short-inversion-time inversion-recovery; TI = inversion time.

regarding obstruction. T2-weighted short-inversion-time inversion-recovery sequences enable assessment of water content to differentiate edematous tissue or cystic structures from other tissue, including fat (3). First-pass perfusion imaging allows assessment of mass vascularity (4), whereas late gadolinium enhancement (LGE) imaging demonstrates the presence of extracellular matrix and is typically absent in the setting of thrombus (5).

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CMR is widely used for mass assessment; however, there have been few studies validating this practice. The study by Pazos-López et al. (6) in this issue of *iJACC* is the biggest to date and provides timely clarification with a unique perspective. They report a retrospective analysis of 116 cases in which they differentiate tumor (n = 42) from thrombus (n = 84), and then benign (n = 17) from malignant (n = 25) tumor, on the basis of CMR tissue characterization with a variety of widely available commercial sequences. On cine imaging, the authors were able to show consistent patterns whereby thrombi were smaller, more homogeneous, and less mobile than tumors (all $p < 0.001$). Compared with normal myocardium, tumors demonstrated signal hyperintensity/isointensity on T2, first-pass perfusion, and LGE (all $p < 0.0001$) with short inversion times (TI), whereas thrombi were hypointense with long TI. On further stratification, benign masses were smaller and had less perfusion and LGE (all $p < 0.03$) than their malignant counterparts. The authors reported that accuracy of differentiation between tumors and thrombi was high at 95%; distinguishing between benign and malignant neoplasms was less accurate at 79%.

T1 mapping is a rapidly expanding CMR technique that has shown utility across a broad range of conditions, particularly in the assessment of myocardial fibrosis. To date, there has been limited use of this novel technique for characterization of intracardiac masses (7). Despite low numbers (n = 30), Pazos-López et al. (6) were able to show a reduction in post-contrast T1 time with tumors compared with thrombi. This finding can be explained by the relative absence of extracellular matrix present in tumor burden compared with soft tissue. However, it seems likely that the T1 value of organized or chronic thrombus might be lower due to increased fibrosis, thereby resulting in less differentiation between the 2

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pathologies. Further validation of this promising technique is required. Fat saturation prepulses are useful adjuncts to standard CMR sequences. They suppress the signal of fatty tissue, which can be useful for differentiation of lipomatous septal hypertrophy, lipomas, and liposarcomas from other cystic or solid cardiac tumors (4). This technique was not routinely used by Pazos-López et al. (6); however, its targeted inclusion in a CMR mass protocol may be useful.

The study by Pazos-López et al. (6) is limited by small study numbers. However, their favorable results suggest that tissue characterization with CMR is worthwhile for improved accuracy in defining cardiac masses. Further prospective data may facilitate validation of a diagnostic algorithm to optimize the CMR sequences used for the greatest accuracy and shortest scan time. Once data are collected from a larger cohort, a more detailed analysis of specific tumor features with CMR tissue characterization may be possible. Our current assessment is limited to determining whether masses are benign or malignant; accurate subtyping remains difficult. Although Pazos-López et al. (6) mention pathological diagnosis as a criteria for differentiation between thrombus and tumor, no data are presented to verify if pathological classification was performed. The absence of histological validation of CMR sequences remains a significant limiting issue of this paper and the technique in general. An important factor, which the paper does not address, is that some patients are unable to receive gadolinium-based contrast due to previous allergy or impaired renal function, which may precipitate nephrogenic systemic fibrosis. Noncontrast CMR may still prove useful in these subjects because multiplanar imaging techniques can overcome the limitations of echocardiographic acoustic windows and allow better assessment of structures, including the right ventricle, pulmonic valve, posterior atria walls, venous drainage, and great vessels. Although computed tomography scans can also be used for assessment of cardiac tumors, their limited functional information and radiation dose give CMR a significant advantage.

Like forensic teams examining for clues, we need to recognize the footprints of specific cardiac masses. A general schema for CMR stratification is listed in **Table 1**. CMR arms the physician detective with additional clues regarding the malignant potential of a mass on the basis of tissue characterization, the intracardiac company that it keeps, and any extracardiac "criminal associates." Pazos-López et al. (6) have provided a timely assessment of CMR accuracy in differentiation between thrombi and benign tumors or malignant intracardiac masses, but ongoing histological validation of CMR sequences is required before further noninvasive subtyping can be performed with certainty. As with criminals, cardiac masses do not always follow the rules, and deferring diagnosis to biopsy remains necessary in many cases.

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