Cardiac MRI: A Useful Tool for Differentiating Cardiac Thrombi from Tumors

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ABSTRACT: **Background:** Correct diagnosis of cardiac masses is a challenge in clinical practice. Accurate identification and differentiation between cardiac thrombi and tumors is crucial because prognosis and appropriate clinical management vary substantially.

Objectives: To evaluate the diagnostic performances of cardiac magnetic resonance imaging (CMR) in differentiating between cardiac thrombi and tumors.

Methods: A retrospective review of a prospectively maintained database of all CMR scans was performed to distinguish between cardiac thrombi and tumors during a 10 year period in a single academic referral center (2004–2013). Cases with an available standard of reference for a definite diagnosis were included. Correlation of CMR differentiation between thrombi and tumors with an available standard of reference was performed. Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy were reported.

Results: In this study, 101 consecutive patients underwent CMR for suspicious cardiac masses documented on transthoracic or transesophageal echocardiography. CMR did not detect any cardiac pathology in 17% (17/101), including detection of anatomical variants and benign findings in 18% (15/84). Of the remaining 69 patients, CMR diagnosis was correlated with histopathologic result in 74% (51/69), imaging follow-up in 22% (15/69), and a definite CMR diagnosis (lipoma) in 4% (3/69). For tumors, diagnostic accuracy, sensitivity, specificity, PPV, and NPV were 96.6%, 98%, 86.6%, 96.2%, and 96.6%, respectively. For thrombi, the results were 93.6%, 86.7%, 98.04%, 92.9%, and 97%, respectively.

Conclusions: CMR is highly accurate in differentiating cardiac thrombi from tumors and should be included in the routine evaluation of cardiac masses.

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KEY WORDS: cardiac MRI (CMR), cardiac mass, cardiac thrombus, cardiac tumor

Correct diagnosis of cardiac masses is a common challenge in clinical practice. Intracardiac thrombi are relatively common [1], while cardiac tumors are less common and are mainly metastatic [2]. Proper differentiation between these two entities is crucial since prognosis and appropriate clinical management vary substantially. Due to the anatomic location, many cardiac masses are not readily accessible for tissue sampling. Moreover, percutaneous biopsy is rarely performed because of the risk of systemic tumor embolization [3]. Thus, imaging plays a key role in obtaining a correct diagnosis.

Transthoracic and transesophageal echocardiography (TTE and TEE) provide accurate imaging but are operator dependent and limited by a restricted field of view and patient habitus. Tissue characterizations by both TTE or TEE is limited as well [2]. Computed tomography (CT) offers detailed imaging, including better tissue characterization, but exposes the patient to ionizing radiation [4]. However, cardiac magnetic resonance imaging (CMR) is superior to CT in both respects [5]. CMR allows combined evaluation of morphology, perfusion, function, and tissue characterization [6]. Thus, CMR may be ideally suited for non-invasive cardiac mass evaluation, specifically to differentiate between thrombi and tumors [7-9]. The body of evidence addressing the accuracy of CMR in the distinguishing between the two growths is limited with relatively few studies available [10-13]. The aim of this study was to determine the ability of CMR to differentiate thrombi from tumors in a consecutive cohort.

PATIENTS AND METHODS

A retrospective review was undertaken of a prospectively maintained clinical database in an academic, tertiary referral center. The database was queried for CMR scans performed for the evaluation of a cardiac mass between 2004 and 2013. CMR findings were evaluated as a consensus diagnosis by two experienced radiologists specializing in cardiovascular imaging.

Imaging evaluation included signal characteristics on cine steady-state free precession (SSFP), pre- and post-contrast T1-weighted turbo (fast) spin echo imaging (T1-TSE), T2-weighted turbo spin echo imaging (T2-TSE), first pass myocardial perfusion imaging (FPP), and myocardial delayed

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enhancement imaging (MDE). On each of these imaging sequences, the signal intensity of the lesion was evaluated as was the homogeneity of the lesion and whether the tumor appeared well-circumscribed or intramyocardial.

Inclusion criteria were:

- CMR referral for the evaluation of a cardiac mass
- Available standard of reference for a definite diagnosis including pathology
- Definite radiological diagnosis or imaging follow-up (CMR, TTE, TEE, positron emission tomography [PET], CT)

Follow-up was obtained by patient chart reviews, imaging studies, and pathology reports.

CMR finding were classified into three categories:

- Anatomical variant
- Benign cardiac finding
- Cardiac mass

Patients in whom CMR ruled out the presence of any pathological finding, or categorized the findings as benign or an anatomical variant, were excluded from further evaluation.

Cardiac masses were further classified into three categories: tumor, thrombus, inconclusive finding. The authors used the original reports, which were blinded to the histologic diagnosis.

The standard of reference for diagnosis was histopathologic report, a definite radiological diagnosis (in cases of cardiac lipoma) [14], or imaging follow-up (CMR, TTE, TEE, PET, CT). All masses were evaluated in two orthogonal planes measuring minimal and maximal diameters. These diameters were correlated with diagnostic accuracy.

The standard of reference for cardiac thrombi diagnosis was histopathologic report or a documented size-reduction/disappearance as a result of anticoagulation therapy, on imaging follow-up (CMR, TTE, CT).

The standard of reference for tumor diagnosis was histopathologic report or a documented significant size-reduction following chemotherapy on imaging follow-up (CMR, TTE, CT).

CMR scans were performed using a 1.5T MRI scanner (Signa HDxt Ver 16 VO2, General Electric, Milwaukee, WI, USA) with a dedicated 8-channel cardiac phased-array coil. A dedicated CMR protocol was applied in all patients and included steady state free precession (SSFP), T2 (5 mm slice width), T1 TSE pre- and post-Gadolinium administration (7 mm slice width), FPP (9 mm slice width, and MDE (7 mm slice width). These sequences were scanned in several relevant planes according to the mass location (axial, short axis, 4, 2, and 3 chamber planes).

STATISTICAL ANALYSIS

Continuous variables were described as mean ± standard deviation and categorical variables as frequency (percentage). Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR-) were reported with 95% confidence interval (WinPepi, version 11.62) [15].

RESULTS

During the study period, 101 consecutive patients (42 males, 59 females; average age 55.4 ± 21.9 years) underwent CMR scans to differentiate between a tumor and thrombus.

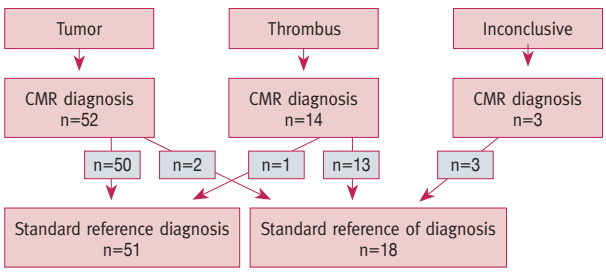
CMR did not detect any suspected lesions in 17/101 (17%). Identifiable CMR findings were documented in 84/101 (83%), representing the study cohort. Anatomical variants were demonstrated in 4/84 (5%). These findings included a sigmoid septum, a prominent ridge adjacent to the left superior pulmonary vein, prominent crista terminalis, and irregularities in the right ventricular free wall. Benign cardiac findings were demonstrated in 11/84 (13%) including interatrial lipomatosis (n=8), mitral annular calcification (n=1), aortic root dilatation (n=1), and a prominent papillary muscle (n=1).

CMR revealed cardiac masses in 69/84 (82%) of the remaining patients, of which 52/69 (76%) were diagnosed as tumors, 14/69 (20%) and were diagnosed as thrombi, while 3/69 (4%) were classified as inconclusive findings according to CMR characteristics.

CMR studies without any findings, anatomical variants, benign findings, and inconclusive findings were not included in statistical analysis.

A correlation of a CMR diagnosis with a standard of reference revealed that two of the 52 cases diagnosed as tumors on CMR were in fact, thrombi, while the other 50 were tumors [Figure 1]. One of the 14 patients diagnosed with thrombi who underwent surgery, was found to have a tumor (leiomyoma originating from the ovarian vein) [Figure 2]. Patient and lesion

Figure 1. CMR diagnosis correlated with standard of reference results. Standard of reference diagnosis was obtained either by pathologic correlation or radiological (TTE, CMR, or CT follow-up as described in the methods section). In the tumor group, two findings were eventually diagnosed as thrombi and in the thrombus group one finding was later diagnosed as a tumor (intersecting arrows)



CMR = cardiac magnetic resonance imaging, CT = computed tomography, TTE = transthoracic echocardiography

characteristics are depicted in Table 1. Tumor characteristics are depicted in Table 2.

Standard of reference for tumors consisted of tissue sampling by cardiac biopsy in 35/51 (68%), tissue obtained from other organs and confirmation with imaging follow-up in 13/51 (25%), and CMR radiological characteristics specific for lipoma 3/51 (7%). The standard of reference for the diagnosis of thrombi consisted of cardiac pathology in 2/15 (13%), follow-up using TTE in 10/15(67%), CMR in 2/15 (13%) [Figure 2], and CT in 1/15 (6%).

Figure 2. Mass in the inferior vena cava (IVC)-right atrium, cardiac MRI (CMR) characterization is consistent with a thrombus. Histology was diagnostic of a leiomyoma. **[A]** Axial steady state free precession demonstrates a hypointense mass in the IVC-right atrium (arrow). **[B]** Coronal T1 post Gadolinium is demonstrated as hypointense compared with the blood in the IVC (arrow). Mass in the left ventricular apex. A follow-up CMR 3 months after anticoagulation treatment demonstrated the mass has resolved, consistent with the diagnosis of a thrombus. **[C]** Four chamber steady state free precession demonstrates a hypointense mass in the apex of the left ventricle. **[D]** Resolution of the apical mass following anticoagulation therapy

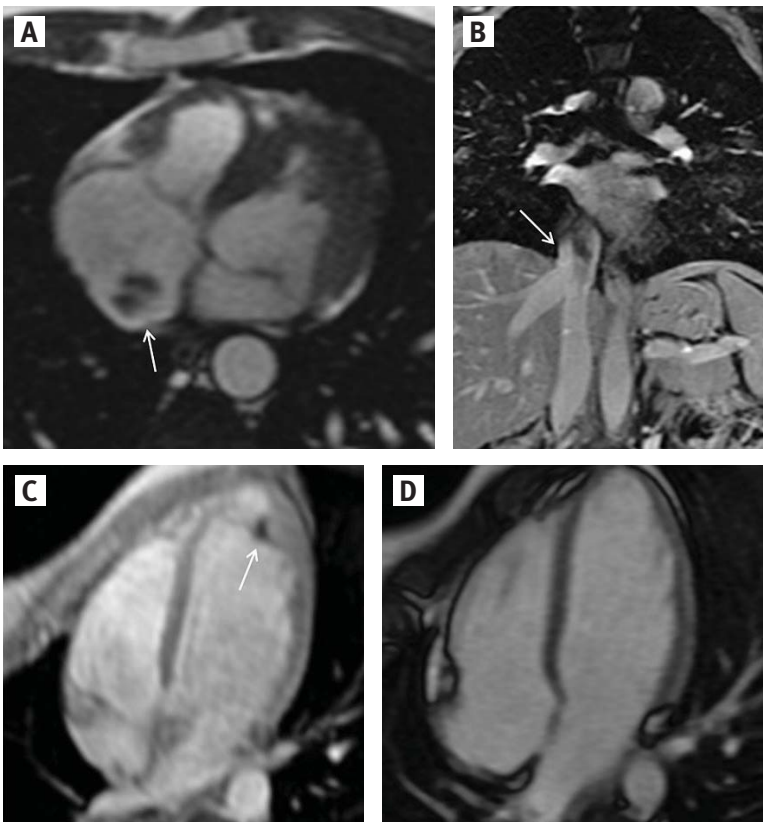


Table 1. Patient and lesion characteristics comparing tumors vs. thrombi

	Tumor	Thrombus
Male:Female	9:6	29:22
Average age, years	57.16	53.39
Average area, cm^2	2058	354.5

For the detection of a tumor, sensitivity, specificity, PPV, NPV, LR+ and LR- was 98% confidence interval (CI) 89.7–99.65, 86.67% CI 62.1–96.26, 96.2% CI 86.8–99.5, 96.6% CI 82.2–99.2, 13.33% CI 3.74–37.88%, and 1.96% CI 0.35–10.3%, respectively.

For the detection of thrombus, sensitivity, specificity, PPV, NPV, LR+ and LR- was 86.68% CI 62.12–96.2%, 98.04% CI 89.7–99.65%, 92.9% CI 66.1–99.8, 97% CI 89.6–99.6, 1.96% CI 0.35–10.3%, and 13.3% CI 3.74–37.8%, respectively. The total accuracy of CMR was 96.3% and 93.6% for tumor and thrombus, respectively.

Of 69 cardiac masses, 48 had a measured minimal diameter more than 10 mm and 21 had a minimal diameter less than 10 mm. A correct diagnosis of thrombus or tumor was obtained in 63 cases, whereas an incorrect or inconclusive diagnosis was made in 6 cases. Of these, four lesions were smaller than 10 mm. Thus, an incorrect diagnosis was more prevalent when lesions were smaller than 10 mm, although this trend did not reach statistical significance ($P = 0.06$).

DISCUSSION

The current study summarizes a large patient cohort demonstrating CMR as highly accurate for differentiating between cardiac thrombi and tumors. This result is in concordance with previous studies suggesting that CMR is a useful modality for differentiating cardiac masses. However, these studies did not incorporate a standard of reference. The largest published study by Pazos-López and colleagues [16] included 116 patients but included a definite diagnosis in only 6%. Fussen et. al. [11] evaluated a cohort of 41 patients, with a pathological diagnosis available in 50%. A high diagnostic pathologic confirmation of 97% was reported by Beroukhim and co-authors [10] but was comprised of a pediatric population. Another recent paper [17]

Table 2. Types of intracardiac tumors

Tumor type	N
Sarcoma	15
Myxoma	11
Lymphoma	8
Hemangioma	5
Lipoma	3
PNET	3
NSCLC	2
Leiomyoma	1
Papillary fibroelastoma	1
Melamona	1
Anaplastic myeloma	1
Total	51

PNET = primitive neuroectodermal tumor
NSCLC = non-small-cell lung carcinoma

evaluated 41 patients with 22 cardiac tumors and 19 thrombi. The standard of reference used by these authors was based solely on a clinical context.

In the present study, CMR proved to be highly accurate in defining cardiac masses, particularly in differentiating cardiac thrombi from tumors. This distinction between cardiac thrombi and tumors is of utmost importance since the therapeutic approach for each entity, whether it is medical or surgical, is completely different. Myocardial CMR characterization is unique in quality and reproducibility. Additional advantages of CMR over other modalities include operator independency, no limitations by patient habitus, no exposure to ionizing radiation, and no iodine administration [6]. Moreover, due to the ability of CMR to accurately diagnose cardiac lipomas, surgery was avoided.

Recent studies evaluating T1 and T2 mapping suggest that parametric mapping holds promise for enhancing the ability of CMR to differentiate between cardiac thrombi and masses [17].

CMR provides exquisite imaging of tumor size and location, adjacent mediastinal structures, and tumor signal characteristics compared with TTE. Although certain characteristics are predictive of a specific pathologic diagnosis such as lipoma, CMR cannot not distinguish between specific tumor types, even when excellent image quality is provided; thus, malignancy might still be difficult to exclude.

The common imaging sequences that are recommended for evaluation of a mass include SSFP, T1-TSE with and without fat suppression, T2-TSE with fat suppression, FPP, and MDE imaging [10]. When an intracardiac thrombus is suspected, post-contrast sequences such as SSFP, T1, and MDE are useful since the thrombi usually do not enhance after contrast administration [10].

The current study suggests a diagnostic limitation for lesions smaller than 10 mm. This difference, however, was not statistically significant, probably because of the small size of this subgroup in our cohort. Therefore, caution should be practiced when evaluating lesions smaller than 10 mm.

CMR excluded any cardiac pathology in 17%. Anatomical variants and benign findings were documented in 17% of the study cohort. CMR was able to correctly characterize incidental findings and differentiate them from a cardiac mass, thus obviating the need for further unnecessary investigations, reducing healthcare system costs, and lowering patient distress in about one-third of the patients.

The current study has several limitations including the retrospective design, the relatively small percentage of thrombi cases, and selection bias. This bias is related to patient referral from multiple institutions, incomplete follow-up, and exclusion from the study cohort. Usually, cardiac thrombi occur at a higher frequency than cardiac tumors [2]. This finding is related to the fact that most of the patients in our cohort were referred for CMR from multiple institutions and follow-up was not available.

Another limitation is the lack of information regarding mass mobility on TTE. Our personal experience suggests that either small sized masses or highly mobile masses might be challenging for CMR detection and characterization. Theoretically, due to inherent CMR technological limitations, small sized, pedunculated tumors that move irregularly during the RR interval might be missed by CMR. We cannot rule out that such cases were not included in our series.

CONCLUSIONS

CMR is highly accurate in differentiating cardiac thrombi from tumors and therefore should be included in the routine evaluation of suspected cardiac masses. CMR diagnostic performance might be reduced in lesions with a minimal diameter smaller than 10 mm.

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