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ADULT CARDIOLOGY

Emerging Role of 3.0 Tesla Cardiac Magnetic Resonance Imaging in Differentiating Cardiac Masses

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ABSTRACT

Objective: To evaluate the role of Cardiac Magnetic Resonance Imaging in differentiating cardiac masses (thrombus vs tumor and benign tumor vs malignant tumor) in local population.

Study Design: Analytical cross-sectional study.

Place and Duration of Study: Tertiary Cardiac Care Center, Department of Cardiac Magnetic Resonance Imaging, Rawalpindi Pakistan, from Oct 2017 to Jun 2021.

Methodology: This retrospective study included (n=56) patients via universal sampling, enrolled for Cardiovascular magnetic resonance imaging with a suspicion of cardiac masses either on echocardiography or Computed Tomography scan. Cardiovascular magnetic resonance imaging sequences were reviewed as SSFP cine images for mass location, size and mobility. T1 weighted turbo spin echo, T2 weighted turbo spin echo with and without fat saturation and TIRM sequences told their intensity as compared to normal myocardium, myomaps evaluated the relaxation time, while contrast first pass perfusion indicated the vascularity and delayed gadolinium enhancement images with standard and long TI were analyzed for contrast enhancement.

Results: Total n=56 patients with a confirmed diagnosis of mass were included for the analysis. Mean age of participants was found to be 45.21(18.3%), height 168.4(8.69%) and weight 68.6(14.94%). There were 47(83.9%) males and females were 9(16.1%). 22(39.3%) had hypertension, 12(21.4%) had diabetes mellitus, 24(42.9%) had previous myocardial infarction. Maximum number of masses were found in LV 31(55.4%) followed by RV 11(19.6%). Sensitivity of T1 map to detect fibrosis in tumor is 100%. Sensitivity of T2 map to detect edema in tumor is 82%.

***Conclusion*:** Cardiac masses like thrombi and tumors are accurately diagnosed by cardiac MRI with etiology.

Keywords: Cardiac magnetic resonance imaging, Cardiac masses, Late gadolinium enhancement, Myomaps.

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INTRODUCTION

Cardiac masses are classified as tumors and thrombi, which are commonly encountered during routine workup. Thrombi are the non-neoplastic lesions. Cardiac thrombi despite their benign nature, can originate in any cardiac chamber in different pathologies. They have high morbidity and mortality rate. Because of their tendency to embolize they are considered to be the high-risk source which can cause stroke. But they have a high preventive potential by anticoagulants. Cardiac tumors are classified as benign tumors, tumors of uncertain biological behavior, germ cell tumor, malignant tumors and pericardial tumors by World Health Organization (WHO) in 2015.[1] Metastatic tumors are almost 20-40 times more common than the primary tumors. Among them only 0.3% are the primary cardiac tumors, out of them 75% are benign tumors and 25% are malignant tumors.[2] Prevalence of primary malignant cardiac tumors was 10.83% among primary cardiac tumors. Myxoma is the most common benign cardiac tumor and sarcoma being the common malignant tumor.[3] Other benign tumors include papillary fibroelastomas, lipomas, fibromas, calcified amorphous tumors, teratomas, hemangiomas, single developmental cysts and rhabdomyomas.[4] In myocardium and pericardium, secondary metastases can take place after direct invasion from breast and lung having primary tumor or if primary tumor is hematogenous either arterial/venous and lymphoid dispersion.[5] A genetic tendency has been acknowledged in certain tumors.[6] They are rare with high morbidity and mortality rates. Among the cardiac masses, thrombi can be treated medically while tumors need surgical resection. Therefore, their clinical differentiation is crucial for appropriate treatment.

Cardiac masses specially tumors were tremendously problematic to diagnose before the epoch of contemporary cardiac imaging modalities. But now they can be evaluated and characterized by multiple

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non-invasive cardiovascular imaging modalities like echocardiography both transthoracic (TTE) and transesophageal (TEE), computed tomography (CT) scan, cardiac magnetic resonance imaging (CMRI) and 18F fluorodeoxyglucose positron emission tomography (18F FDG-PET).[7] Main aim of these non-invasive diagnostic imaging techniques is to identify the mass, its location, size, extent and vascularity, and assist in planning the treatment. The first prerequisite of each imaging technique dealing with the diagnosis of cardiac masses is to precisely differentiate between a tumor and a thrombus. Secondly, accurate knowledge of cardiac anatomy and normal variants is crucial for the observer reporting the scans, because with the advent of advance techniques, normal deviations can be picked as abnormality more recurrently and effortlessly by an inexperienced worker.

Primary imaging modality that is used to evaluate cardiac masses is echocardiography because of its wide availability and easily operatable, but with few limitations like operator dependent, limited tissue characterization and restricted acoustic window. To overcome these limitations, Computed Tomography (CT)-scan will be the modality of choice to evaluate cardiac masses but at an expense of radiation exposure. It can evaluate infiltration and fibrosis by calculating extracellular volume.[8] Contrast enhancement patterns help in differentiating cardiac masses.

In contrary to these, (Magnetic resonance imaging) MRI is the advance imaging modality with no ionizing radiation exposure, high contrast resolution and better soft tissue characterization for the assessment of cardiac masses. With the wide range of sequences, MRI accurately describe the morphology, composition and perfusion of the cardiac masses.[9,10] Thrombus and tumor can be effectively differentiated by enhanced MRI scan.

However, studies on Cardiovascular magnetic resonance imaging (CMR) role in diagnosing cardiac masses are scant with a small sample size. This study was designed to evaluate the role of CMR in differentiating cardiac masses with a variety of sequences. It analyzes cardiac masses both qualitatively (morphology and intensity) and quantitatively (parametric mapping).

METHODOLOGY

We opt universal sampling technique in this descriptive cross-sectional study and retrospectively reviewed scans of (n=56) patients. This study was conducted after the approval of institutional review board (IERB letter # 26/1/R&D/2022/143).

Sample Size: All the patients who underwent diagnostic modalities during study period were included in the study and they accounted to n=56.

Inclusion Criteria: All patients including both gender, male and female, underwent CMR after the evidence or suspicion of mass on either imaging modality from October, 2017 to June ,2021 at CMR department of a Tertiary Cardiac Care Center in Rawalpindi Pakistan.

Exclusion Criteria: Patients with vegetation, cardiomyopathies, left ventricular failure and non-compatible 3.0T MRI metallic implants.

Cardiac MR studies were performed on 3.0 Tesla Siemens Magnetom Skyra with dedicated 18 channel phased array surface coils which were used as receivers. Protocol designed to evaluate cardiac masses included following sequences: SSFP Cine images, TIRM, T1-weighted and T2-weighted turbo spin echo with SPAIR fat saturation, T1 and T2 weighted Myomaps, first pass perfusion, and late gadolinium enhancement with standard and long TI images. All the sequences were attained during expiratory breath hold and with ECG gating. 0.15 mmol/kg dose of a contrast gadopentetate dimeglumine (Gadovist 1.0 mmol/ml) is used. On an average 1.5 hours was required for scanning.

The mass was categorized as a tumor or thrombus, and tumor was then further classified as benign or malignant. Mass lesion that appeared hypointense on long TI (900ms) images was considered as thrombus and the rest were marked as tumors. Tumors were differentiated as benign or malignant on the basis of their shape, location and signal intensity on cine images (SSFP), T1W TSE, T2W TSE, TIRM and LGE images. Myomaps were used for quantitative assessment.

Mass was evaluated on CMR with following image characteristics:

- Mass appearance before contrast.
- Morphology (location, area and mobility on cine images).
- On T1W, T2W and TIRM images, signal intensity was analyzed qualitatively as isointense, hypointense or hyperintense as compared to normal myocardial intensity.
- On T1 and T2 parametric maps, relaxation times were noted for quantitative analysis.
- On first pass perfusion images, contrast uptake was assessed after gadolinium contrast agent administration.

- TI scout (look-locker) sequence was used to identify the inversion time of a normal myocardium to be nulled.
- On phase sensitive inversion recovery images, presence of LGE was assessed.

Starting with the SSFP bright blood cine imaging, single slice of 2, 3, 4 chamber and 9-12 slices of short axis depending upon heart size were obtained with TR of 37.3ms, TE of 1.16ms, matrix size 153x240, a flip angle 800 and band width of 947. T1W TSE, T2W TSE and TIRM sequences with black blood images were obtained along long and short axis of the mass with TR of 550, 800, 800ms, TE of 29, 75, 44ms, matrix size of 192x256, 192x256, 125x256, flip angle of 1800, 1800, 1800, echo spacing of 4.1, 3.88, 5.49ms and a band width of 849, 781, 849 respectively along with the SPAIR fat saturation. First pass perfusion (FPP) gradient echo sequence will be run with the TR of 160.2 ms, TE of 1.08ms, matrix size of 96x160, flip angle of 120, band width of 651 and echo spacing of 2.5ms. Late gadolinium enhancement (LGE) bright blood gradient echo sequence has a TR 800ms, TE 2.75ms, flip angle 250, matrix size 153x240, band width 140 and echo spacing of 7.7ms, with a standard TI ranging from 270-330 (identified by TI-scout images) and a long TI of 900ms.

New emerging MRI technique was parametric mapping. Parametric T1 map before contrast was a trufi sequence with a TR of 280.5ms, TE of 1.12ms, matrix of 126x256, flip angle of 35°, band width of 1085, inversion time(TI) of 180ms and echo spacing of 2.6ms. Pre-contrast parametric T2 map was a gradient echo sequence with a TR of 194.7ms, TE of 1.29ms, matrix size of 108x192, flip angle of 12°, band width of 1184, echo spacing of 3.1ms and with three T2 prep intervals at 0, 30, 55ms.

SPSS-23.0 was used for data analysis. Categorical data was analyzed as frequency and percentage, and continuous variables as mean and standard deviation. Chi square test was used to assess the differences in CMR features between tumor and thrombus and between benign and malignant.

RESULTS

Total (n=56) patients with a confirmed diagnosis of mass were included for the analysis. Demographics and clinical characteristics of participants along with cardiac masses location and CMR features are presented in Table-I. Mean age of participants was found to be 45.21±18.3 years, height 168.4+8.69 cm and weight 68.6±14.94 kg. There were 47(83.9%) males and females were 9(16.1%). 22(39.3%) had hypertension, 12 (21.4%) had diabetes mellitus, 24(42.9%) had previous myocardial infarction. Maximum number of masses were found in LV 31(55.4%) followed by RV 11(19.6%).

Table-I: Demographics and Clinical Findings of Cardiac Masses on CMR (n=56)

Variables		n(%); Mean±SD
Age (Mean±SD)years		45.21±18.3
Height (Mean±SD)cm		168.4±8.69
Weight (Mean±SD)kg		68.6±14.94
Gender	Male	47(83.9%)
	Females	9(16.1%)
Co-morbidities	HTN	22(39.3%)
	DM	12(21.4%)
	Previous MI	24(42.9%)
	Myocardial Scar	25(44.6%)
	Pericardial Effusion	5(8.9%)
Location	LV	31(55.4%)
	RV	11(19.6%)
	LA	6(10.7%)
	RA	2(3.6%)
	LV,RV	2(3.6%)
	LA,LV	1(1.8 %)
	Pericardium	3(5.4%)

LV= Left Ventricle; RV= Right Ventricle; LA= Left Atrium; RV= Right Atrium

Chi Square test was applied and the association of CMR features mobility, steady state free precession (SSFP), T1-weighted turbo spin echo (T1W TSE), T2-weighted turbo spin echo (T2W TSE), turbo inversion recovery magnitude (TIRM), first pass perfusion (FPP) and late gadolinium enhancement (LGE) with long TI among the cardiac masses was found to be statistically significant (Table-II).

Table-II: Association Between CMR Features and Cardiac Masses

CMR Features	Thrombus	Benign tumor	Malignant tumor	*p*-value
Mobility	4(10.5%)	6(60%)	3(37.5%)	0.003
SSFP(hyperintense)	0(0%)	2(20%)	1(12.5%)	0.028
T1W TSE (hyperintense)	6(15.8%)	4(40%)	3(37.5%)	0.16
T2W TSE (hyperintense)	6(15.8%)	8(80%)	4(50%)	0.001
TIRM (hyperintense)	5(13.2%)	10(100%)	8(100%)	0.001
FPP	0(0%)	7(77.8%)	8(100%)	0.001
LGE(long TI)	0(0%)	8(88.9%)	8(100%)	0.001

T1W TSE=T1-weighted turbo spin echo, T2W TSE=T2-weighted turbo spin echo TIRM=turbo inversion recovery magnitude,FFP= first pass perfusion, LGE=late gadolinium enhancement

Total 55 patients were analyzed with FPP and LGE. Parametric T1and T2 maps were available for 53-scans. Their association with cardiac masses is listed in Table-III.

Table-III: Association between Pre-contrast Parametric Mapping and Cardiac Masses

Mapping		Thrombus n=38	Benign Tumor n=10	Malignant Tumor n=8	*p*-value
T1 Map	<1100	3(8.3%)	0(0%)	0(0%)	0.14
	1101-1250	4(11.1%)	0(0%)	0(0%)	
	1251-1400	13(36.1%)	1(11.1%)	1(12.5%)	
	>1400	16(44.4%)	8(88.9%)	7(87.5%)	
T2 Map	<30	0(0%)	0(0%)	0(0%)	0.007
	31-45	13(36.1%)	0(0%)	2(25%)	
	46-60	15(41.7%)	1(11.1%)	3(37.5%)	
	>60	8(22.2%)	8(88.9%)	3(37.5%)	

Accuracy of CMR sequences for the diagnosis of thrombus vs tumor is listed in Table-IV. LGE with long TI is the most sensitive and specific sequence in differentiating tumor vs thrombus.

Table-IV: Accuracy of CMR Features for the diagnosis of Thrombus vs Tumor

CMR Feature	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Mobility	33	89	69	79	76
T1W	38	76	53	74	69
T2W	66.6	84	66	84	78
T1 Map (pre-contrast)	100	19.4	36	100	45
T2 Map	87	25	37	80	46
FPP	88	72	72	95	72
LGE	94	100	100	97	96

Sensitivity of T1 map to detect fibrosis in tumor is 100%. Sensitivity of T2 map to detect edema in tumor is 87%.

DISCUSSION

The diagnostic precision of cardiac MRI features is established by the current study, for the differential diagnosis of thrombus vs tumor and benign vs malignant tumor. Thrombi are mostly small in size with homogenous texture. According to López *et al*. almost 80% thrombi are immobile,[11] which is supported by current study by stating 89% thrombi as immobile. Mean area of thrombi is 2.4cm^2 in this study, which was reported as that of 1.6cm^2 and 1.9cm^2 by Weinsaft *et al*. and Mohrs *et al*. respectively.[12,13] Antithrombotic therapy is considered to be the main source of this small size of a thrombus. Malignant tumors are larger in size as compared to benign tumor. This feature is also consistent with the previous studies.[14]

Lesion texture, homogenous and heterogenous, was not considered as a distinguishing feature in previous studies. 99% thrombi were stated as homogenous lesions, whereas only one-half tumors appear to be homogenous which can be explained with the difference in tissue composition. According to some previous studies texture was thought to be the distinguishing characteristic to diagnose malignant tumors but with the advent of advance and sensitive imaging modalities, this was proven wrong as some of benign lesions specially myxomas were heterogenous as well.[15] Now a days, it did not prove as a diagnostic feature to differentiate masses and it is supported by this study as well. Tumors are more mobile than thrombi but it is also not a characteristic feature to diagnose thrombu s and tumor.

Cardiac tumors usually occur at a specific location and structure. Myxomas and sarcomas mostly develop in left atrium(LA) while angiosarcomas occur at right atrium(RA).[16] Rhabdomyomas and fibromas develop in ventricles whereas, papillary fibroelastomas appear on the valves.[17] In the end, metastatic tumors, depending upon cancer spread, can be found anywhere in the heart.[18] As this current study has small sample size mainly of tumors, it is bit difficult to compare tumor location classification with other studies. But 5(71.4%) myxomas were found in LA in current study.

Frequency of hyperintensity on T2W TSE sequence is more for tumors than thrombi but few clots also appeared as hyperintense on T2W images. Subacute clots appear as hyperintense on T1W and T2W images due to red blood cell lysis and presence of deoxyhemoglobin and methomoglobin. Chronic thrombi are isointense or hypointense due to replacement with fibrosis tissues. Most of the benign and malignant tumors are hypointense or isointense on T1W and hyperintense on T2W images.

Thrombi are mostly hypointense on first pass perfusion due to avascular nature. However, some show vascularity in chronic stage but in current study no thrombus shows vascularity. Benign lesions show heterogenous perfusion due to sparse vascularity while heterogenous perfusion with dense vascularity is being shown by malignant tumors.[19]

In 100% of our thrombi population, late gadolinium enhancement is absent, which was 95% stated by López *et al.* Therefore, thrombi can be easily differentiated from tumors after contrast injection as thrombi appear hypointense whereas, tumor appear hyperintense or isointense and can be confirmed with long TI on the basis of their intensity.

In differentiating thrombus vs tumor, FPP and LGE are more sensitive and accurate with sensitivity of 96% and 95% and accuracy of 85% and 87% respectively according to López *et al.* which are in concordance to present study stated sensitivity and accuracy as 88% and 72% for FPP and 94% and 96% for LGE respectively. Assessment of mobility on CMR showed accuracy of 76% relative to previous study with accuracy of 69%. T2W sequence of CMR is more specific (84%) and accurate (78%) according to current study. Previous studies showed similar results with specificity of 85% and accuracy of 71%.[11]

Twenty (50%) of thrombi show native parametric T1 time less than 1400ms while 8(88.8%) of benign tumors and 7(87.5%) of malignant tumors show time of more than 1400ms. Thrombi depict low T2 time as compared to both benign and malignant tumor.[20] This study shows 73.6% (28) thrombi and 62.5% (5) malignant tumors have T2 time less than 60ms and only 20% (2) benign lesions have less than 60ms T2 time. Majority of benign tumors show parametric T1 time ranging from 2000-2750ms, malignant tumors have T1 time in between 1450-1950ms whereas, thrombi lie within 600-1650ms. Parametric T2 time for thrombi is 30-80ms, for benign tumor is 70-130ms and for malignant tumor is 40-85ms.

LIMITATIONS OF STUDY

Sample size was quite low thus, the significant differences in CMR features was absent possibly related to low statistical power. Study should be a multicenter study as there is low prevalence of cardiac tumors. It is difficult to differentiate tumor subtypes. CMR features are influenced by subjectivity as they were evaluated qualitatively instead of quantitative assessment. Larger studies to quantify cardiac masses are desirable as it was limited due to small size and excessive motility in some cases.

CONCLUSION

The etiology of cardiac masses may be unclear after echocardiography and CT scan while CMR features are more sensitive to differentiate them. It is due to vast range of sequences of MRI. Cine images accurately describe about their location, morphology and extent. Dark blood turbo spin echo images tell us about their morphology and help in differentiation on the basis of their intensities. Vascularity of a tumor is assessed by first pass perfusion. Myomaps are the new emerging sequences that aid in tumor differentiation without contrast. Finally late gadolinium enhancement images differentiate cardiac masses with high accuracy with the help of long T1 i.e., 900ms at 3T.

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Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MS: Intellectual contribution, concept and final approval

GRM: Intellectual contribution, concept & final approval

JK: Analysis, manuscript writing and proof reading

NS: Data collection, data analysis and review of article

WUR: Proof reading, Intellectual contribution, final approval

AAC: Intellectual contribution, concept & final approval

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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