Original Article

Appropriateness and diagnostic yield of cardiac magnetic resonance imaging from a tertiary referral center in the Middle East

Wael AlJaroudi[1,2]*, Hussain Isma'eel[1,3]*, Fadi El Merhi[2], Tony Assad[2], Mukbil Hourani[2]

[1]Division of Cardiovascular Medicine, [2]Division of Radiology, American University of Beirut Medical Center, Beirut, Lebanon; [3]Heart and Vascular Imaging Institute, Cleveland Clinic, Cleveland, Ohio, USA

*These authors contributed equally to this work.

Correspondence to: Wael AlJaroudi, MD, FESC, FACC. Assistant Professor of Medicine and Diagnostic Radiology, Division of Cardiovascular Medicine and Radiology, American University of Beirut Medical Center, Riad El-Solh 1107-2020, Beirut, Lebanon. Email: wa53@aub.edu.lb.

Purpose: Cardiac magnetic resonance imaging (CMRI) is a novel non-invasive modality with many potential indications, and was recently introduced in Lebanon. We sought to assess the appropriateness and diagnostic yield of CMR studies performed at a tertiary referral center from the Middle East since the inception of the program.

Methods: All patients who underwent CMR studies between January 1st 2013 and June 18th 2014 were enrolled in this study. CMR reports were retrospectively reviewed. The study indication, clinical history, and findings were extracted and analyzed. The appropriateness of the study was judged according to the 2010 updated Asian Society of Cardiac Imaging guidelines.

Results: There were a total of 142 patients [mean age 42.1 (SD: 18) years, 24.6% females] that underwent CMR study. Two-thirds of studies were performed on an outpatient basis, and outside referrals constituted 16.2% of the entire cohort. The cardiologists referred 122 cases (86%) with main contribution from electrophysiology and imaging specialists. Of the 142 cases, 12 (8.4%) were not indicated and added little value. Of the remaining 130 appropriate studies (appropriateness level A8-A9), one-third had an incorrect diagnosis prior to CMR, and 8% had relevant findings that were missed on other studies but captured by CMR. Furthermore, CMR confirmed the diagnosis in 28% of the cases, provided relevant information on scar burden, shunt quantification, and ruled out infiltrative disease in the remaining patients. Also, CMR demonstrated the presence of scar in 45 of patients, among whom 20 (44%) had significant scar volume quantification (>5% of left ventricular myocardium). Finally, 9% of patients had a relevant extra-cardiac finding that needed further investigation.

Conclusions: Despite the recent launch of the CMR program at our institution, the majority of studies were appropriately indicated, provided relevant data and were clinically useful. Inappropriate or uncertain studies did not provide relevant data, and should be further minimized to avoid unnecessary costs and downstream testing. Large prospective CMR database with clinical follow-up is needed to provide more insight about cardiovascular disease and outcomes in our population.

Keywords: Appropriateness; diagnostic yield; cardiac magnetic resonance imaging (CMRI); Middle East

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Introduction

Cardiac magnetic resonance imaging (CMRI) is a novel non-invasive imaging modality that was introduced in clinical practice since the 1990's. It provides high quality images with pertinent information on anatomy, tissue characterization, function, hemodynamics, and others (1). Its clinical applications have expanded over time and include detection of coronary artery disease (2-4), viability and scar burden (5), differentiating types of cardiomyopathy (6-10), assessment of cardiac masses and vascular structures (11). It also provides the tools for risk stratification and guiding therapy (12,13).

In order to standardize the utilization of this modality and avoid unnecessary testing, and under the auspices of the American College of Cardiology Foundation (ACCF), together with key specialty and subspecialty societies (including Society of CMR), that the 2006 appropriateness criteria were developed (14). They were then adopted and updated by the Asian Society of Cardiac Imaging in 2010 (15). The technique however, was only recently introduced in the Middle East and is not readily available except at few academic tertiary centers. In Lebanon, a comprehensive CMR program was launched on January 1st 2013 at our institution. The test is relatively (16) expensive and often represents a financial challenge to patients and third party payers, particularly with such economic constraint in the society. Hence, we sought to assess the appropriateness of CMR testing at our institution since its inception and over the first year and a half; and to evaluate the clinical yield of the studies in order to optimize future performance, provide standard of care testing in compliance with the guidelines, and avoid unnecessary testing.

Methods

Patient selection

All patients that underwent clinical CMR between January 1st 2013 [starting date of the launch of the comprehensive CMR program at the American University of Beirut Medical Center (AUBMC)] and June 18th 2014 were included in the study. None of the patients were excluded. Patients' demographics (age, gender, body mass index), referral pattern, specialty of the referring physicians, indication, clinical findings including the presence of incidentals were retrospectively extracted from the report. The study was approved by the Institutional Review Board at AUBMC.

Cardiac magnetic resonance imaging (CMRI)

CMR studies were performed on Philips Ingenia 3.0 T and 1.5 T release 4.1.1 (Eindhoven, Netherlands) scanners. The latter was reserved for patients with suspicion of cardiac siderosis. Prior to the imaging, a cardiologist (Wael AlJaroudi, Hussain Isma'eel) reviewed the request, clinical indication and patient history, in order to set up the appropriate CMR protocol, but without excluding any request (hence minimizing selection bias). Turbo spin echo and gradient echo images were obtained for anatomic definition, while dynamic cine images [balanced fast field echo (B-FFE)] for the evaluation of cardiac function and valvular analysis. Phase contrast was used to assess hemodynamics, calculate flow and shunt fraction. On selected patients and depending on the indication, contrast enhanced volumes sets were acquired for 3-D MRA (magnetic resonance angiogram) reconstructions after use of gadolinium dotaram (0.5 mmol/mL, 0.1 mmol/kg) with advanced off-line 3-D post-processing using multiplanar reconstructions for optimal morphologic evaluation. Delayed gadolinium-enhancement (phase sensitive inversion recovery) analysis was performed to assess for viability, scar volume quantification (using standard semi-automated method) and infiltrative disease. Finally, for patients with clinical suspicion of iron overload, T2* imaging (turbo fast echo with multiple echoes) was performed to assess for iron content in the heart and liver.

Appropriateness

All CMR reports were retrieved and retrospectively reviewed by a level III CMR trained and certified physician (Wael AlJaroudi). The clinical history, indication of the CMR study and findings were extracted from the CMR report. The indications were coded according to the 2010 updated Asian Society of Cardiac Imaging guidelines with their corresponding appropriateness level {A [7-9]: appropriate; U [4-6]: uncertain; I [1-3]: inappropriate} (*Table 1*) (15). Given the close similarity of these guidelines to the 2006 multi-society appropriateness criteria (14), coding and analyzing the data using the other guidelines yielded same appropriate utilization rate.

Diagnostic yield

The usefulness of the CMR study was judged on whether if fulfilled any of the following pre-specified criteria: (I) provided relevant findings that were missed or could not be detected on transthoracic echocardiogram; (II) confirmed a clinical diagnosis that was suspected on other imaging modality; (III) corrected a diagnosis that was falsely made prior to the CMR; (IV) provided accurate evaluation and quantification that have impact on guiding therapy; (V) provided information on scar burden for risk factor stratification; (VI) ruled out infiltrative cardiomyopathy; or (VII) was not helpful and did not add any relevant information. Incidental extra-cardiac findings were also documented and extracted for analysis.

Table 1 Summary of the most common indications and appropriateness level from the 2010 updated Asian Society of Cardiac Imaging guidelines

Indication number	Indication	Appropriateness level
35	Assessment of complex congenital heart disease including anomalies of coronary circulation, great vessels, and cardiac chambers and valves	A8
36	Assessment of post-operative congenital heart disease, such as residual pulmonary stenosis, ventricular septal defect, and patency check for Blalock-Taussig shunt	A8
37	Evaluation in patients with new onset heart failure to assess etiology	A8
41	Evaluation of specific cardiomyopathies (infiltrative (amyloid, sarcoid), hypertrophic, cardiotoxic therapy)	A9
43	Evaluation of arrhythmogenic ventricular cardiomyopathy; patients presenting with syncope or ventricular arrhythmia	A8
44	Evaluation of myocarditis or myocardial infarction with normal coronary arteries; positive cardiac enzymes without obstructive atherosclerosis on angiography	A9
45	Evaluation of cardiac mass (suspected tumor or thrombus); patients with technically limited images on echocardiogram	A9
46	Evaluation of pericardial conditions	A8
48	Determine location and extent of myocardial infarction, including no reflow zone; post-acute myocardial infarction	A9
50	Determine viability prior to revascularization	A9

Statistical analysis

Continuous data were expressed as a mean ± one standard deviation or median (25th and 75th percentile), while categorical data were displayed as frequencies and percentage. Pie and bar diagrams were used for figure illustration. All statistical analyses were performed using the Statistical Package for Social Sciences, version 19, for Windows (SPSS, Chicago, Illinois, USA).

Results

Patient characteristics

A total of 142 patients [mean age 42.1 (SD: 18) years, 24.6% females] underwent CMR between January 1st 2013 and June 18th 2014 (*Table 2*).

Pattern of referral

Almost two-thirds of studies were performed on an outpatient basis. Referrals from within the institution constituted the majority of cases (83.8%), with 16.2% of the studies being referred from other hospitals and private practices. The specialty and sub-specialty of the referring physicians are illustrated in *Figure 1*. The cardiologists referred 122 cases (86%) with main contribution from electrophysiology and imaging specialists, followed by the interventional and heart failure.

Appropriateness of CMR studies

The indications of the CMR studies are summarized in *Figure 2*. The most common ones included assessment of specific cardiomyopathies (infiltrative, amyloid, sarcoid, hypertrophic, post-cardiotoxic therapy), arrhythmogenic right ventricular dysplasia, myocarditis, and congenital cases. CMR studies to assess for new onset heart failure etiology, viability, cardiac masses and pericardial diseases constituted the remaining 21.9% of the studies. The appropriateness level for each of the indication is listed in *Figure 2* (A8-A9). There were an additional of 12 cases (8.4%) that were referred for seemingly appropriate indications; however, on careful review of the clinical history, they were deemed as uncertain or inappropriate. The details of these 12 cases are summarized in *Table 3*. The appropriate utilization rate was similar when using the 2006 multi-society guidelines (14).

Diagnostic yield

Of the 142 CMR studies, 12 were considered to have

Table 2 Patient characteristics

Characteristics	Statistical results
Demographics	N=142
Age, years	42.1±18
Female	35 (24.6%)
Body mass index, kg/m^2 (n=112)	27.0 (24.2-30.2)
Body surface area, m^2 (n=129)	2.0 (1.8-2.1)
CMR study	
Outpatient	97 (68.3%)
Outside referral	23 (16.2%)
Referred by cardiologist	123 (86.6%)
Left ventricle	
Left ventricular end diastolic volume, mL (n=130)	163.5 (147.8-203.3)
Left ventricular end systolic volume, mL (n=130)	75.0 (57.8-102.5)
Left ventricular ejection fraction, % (n=130)	55.0 (48.9-59)
Left ventricular cardiac output, mL/min (n=125)	5.9 (4.95-7.20)
Right ventricle	
Right ventricular end diastolic volume, mL (n=94)	166.5 (141.0-198.3)
Right ventricular end systolic volume, mL (n=94)	78.5 (62.0-101.3)
Right ventricular ejection fraction, % (n=94)	53.0 (48.0-58.0)
Valvular heart disease (≥ moderate stenosis or regurgitation)	15 (10.7%)
Delayed gadolinium enhancement imaging (n=120)	
Positive late gadolinium enhancement	45(37.5%)
Late gadolinium enhancement of the pericardium or right ventricle	3 (2.5%)
Left ventricular scar 0%	75 (62.5%)
Left ventricular scar 1-5%	22 (18.3%)
Left ventricular scar 6-10%	7 (5.8%)
Left ventricular scar >10%	13 (10.8%)
Relevant extra-cardiac incidental findings	19 (13.3%)

CMR, cardiac magnetic resonance.

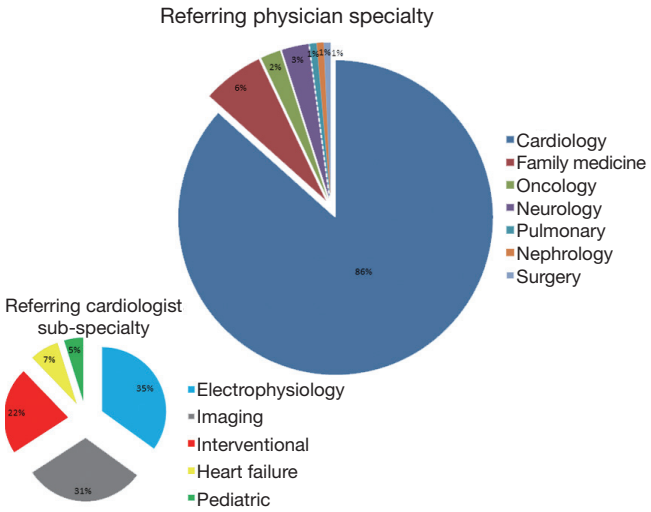

Figure 1 Pie chart illustrating the specialty of the referring physician for the cardiac magnetic resonance imaging. The cardiologists represented the majority of the physicians (86%), among whom the electrophysiology and imaging subspecialists contributed to two-thirds of the referrals.

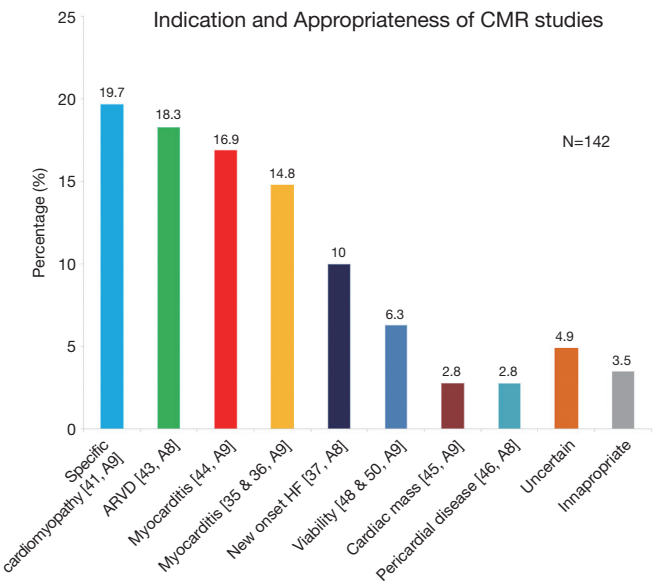

Figure 2 Bar diagram illustrating the indications (percentage) for all the CMR studies that were performed. The indication for each study was coded according to the 2010 updated Asian Society of Cardiac Imaging guidelines with their corresponding appropriateness level. CMR, cardiac magnetic resonance.

Table 3 Details of non-appropriate indications for CMR studies

Original indication	Appropriateness	Details
44-myocarditis	Uncertain	Patient had prior CMR showing myocarditis (LGE 15% LV) and mildly reduced EF. Follow-up echocardiogram showed normal EF. Follow-up CMR was ordered to assess residual LGE for risk stratification
44-myocarditis	Uncertain	Patient had prior CMR showing myocarditis (LGE 10% LV) and normal EF. Follow-up CMR was ordered to assess residual LGE for risk stratification
43-ARVD	Uncertain	Positive family history of SCD. Normal echocardiogram. Concern for ARVD. No syncope or VT
43-ARVD	Uncertain	Patient with VT. Normal echocardiogram. CMR ordered to rule out scar or focus or arrhythmia
41-specific cardiomyopathy	Uncertain	Palpitation and presyncope. Normal echocardiogram. Rule out scar or infiltrative disease
43-ARVD	Uncertain	Patient had prior CMR showing minor ARVD criteria with frequent PVCs and low EF. CMR ordered post ablation to assess for scar at the site of ablation and improvement in EF
38-LVEF in heart failure	Uncertain	Patient had an echocardiogram—did not add much information
45-Mass	Inappropriate	Echocardiogram clearly showed prominent Chiari network and not right atrial mass
43-ARVD	Inappropriate	Dizziness-concern for ARVD. Normal echocardiogram. No syncope or VT
43-ARVD	Inappropriate	Brother died while swimming. R/o ARVD. Normal echocardiogram. No VT or syncope
43-ARVD	Inappropriate	Palpitation with normal echocardiogram. Rule out scar or fibrosis
46-pericardial disease	Inappropriate	First episode of pericarditis. Negative cardiac enzymes. CMR ordered to assess for pericardial and myocardial LGE

ARVD, arrhythmogenic ventricular dysplasia; CMR, cardiac magnetic resonance imaging; EF, ejection fraction; LGE, late gadolinium enhancement; LV, left ventricle; SCD, sudden cardiac death; VT, ventricular tachycardia.

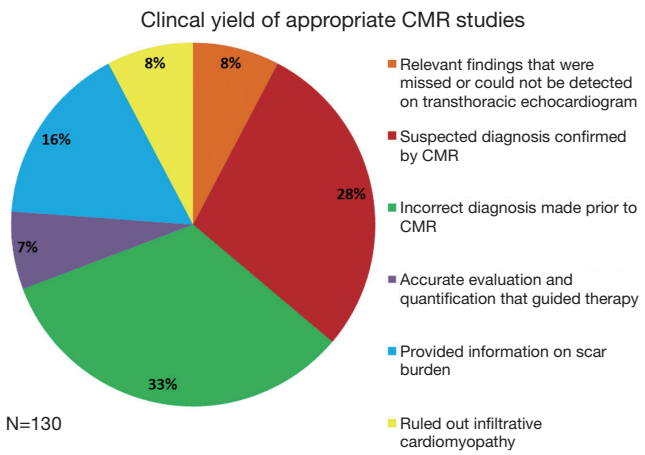

Figure 3 Pie diagram illustrating the clinical yield of all appropriate CMR studies (N=130). None of the uncertain or inappropriate studies yielded clinically relevant results (N=12). CMR, cardiac magnetic resonance.

uncertain or inappropriate indications, and none of them provided any additional information beyond the echocardiogram or clinical history. Of the remaining 130 appropriate cases, the diagnostic yield of the studies is summarized in *Figure 3*. Almost one-third of cases had an incorrect diagnosis prior to CMR. An additional of 8% of cases had relevant findings that were missed on other studies (example anomalous pulmonary veins, sinus venosus defect, etc.). In addition, CMR helped confirm the diagnosis in 28% of cases, and provided accurate quantification to guide optimal therapy (for example, quantification of pulmonary regurgitation fraction and right ventricular end-diastolic volume index to guide optimal timing of pulmonary valve replacement in patients with tetralogy of Fallot; shunt fraction; quantification of ejection fraction to decide on implantable cardiac defibrillator) (*Figure 4*).

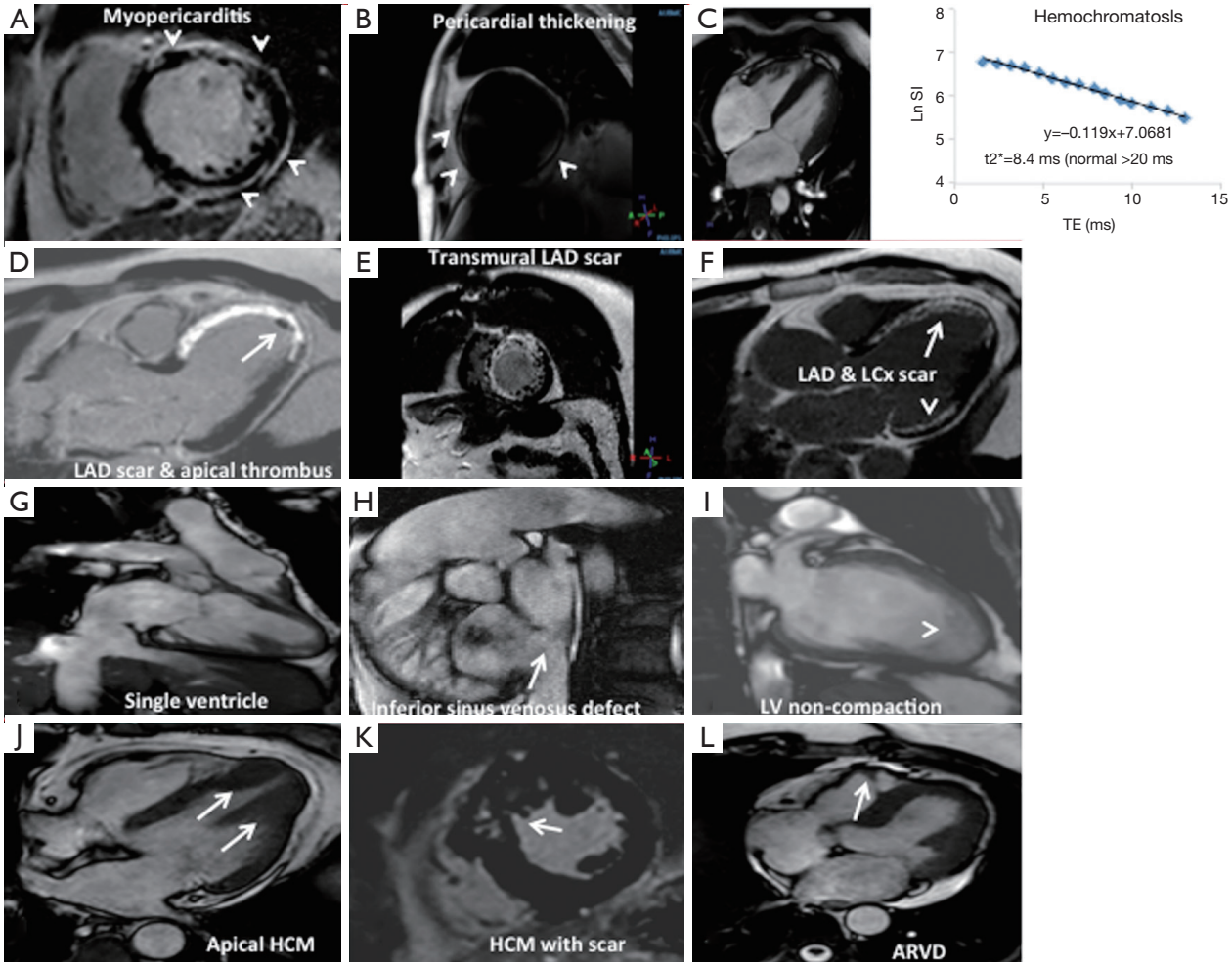

Figure 4 Illustrative examples of several CMR cases that confirmed or changed diagnosis. (A) A case of myopericarditis confirmed by CMR (arrow heads delineating areas with late Gd enhancement); (B) is a case of constriction with evidence of pericardial thickening on T2 imaging; (C) illustrates the case of a patient with liver cirrhosis and normal echocardiogram with EF 60% (confirmed also by CMR); however, T2* imaging showed significant signal decay and short T2* of 8.4 ms (normal >20 ms) consistent with moderate cardiac siderosis and confirming the diagnosis of hemochromatosis; (D) showed significant transmural scar in the left anterior artery (LAD) distribution; there was however evidence of apical thrombus (arrow) that was missed on echocardiogram and that required change in anticoagulation management; (E) showed transmural scar in the LAD and no viability in the area; revascularization of the LAD was not recommended accordingly; (F) showed two different ischemia scar; transmural LAD scar that was known (arrow) and a subendocardial scar in the left circumflex artery (arrow head) that was not previously known; (G) is a complex congenital case of a single ventricle with pulmonary and sub-infundibular stenosis and atretic systemic ventricle; (H) is a patient with dilated right atrium and ventricle on echocardiogram without obvious cause; CMR confirmed inferior sinus venosus defect with a communication between the inferior vena cava, left and right atrium; (I) is a patient with arrhythmia, poor echocardiographic images and clear evidence of LV non-compaction (arrow head); (J) is a case of apical hypertrophic cardiomyopathy (arrow) that was missed on echocardiogram; (K) is a panel with hypertrophic cardiomyopathy that had syncope and evidence of scar on LGE (arrow); CMR helped risk stratify the patient and an implantable cardiac defibrillator was recommended; (L) is a patient with non-sustained ventricular tachycardia, positive family history of sudden cardiac death, suspicious echocardiogram, and CMR cine imaging that showed focal dyskinetic segment of the right ventricular free wall (arrow), confirming the diagnosis of arrhythmogenic right ventricular dysplasia. CMR, cardiac magnetic resonance imaging; EF, ejection fraction; LV, left ventricle; LGE, late gadolinium enhancement.

Table 4 Relevant extra-cardiac incidental findings

Extra-cardiac finding	Number of cases (%)
Breast nodules	1 (0.7)
Lung mass or nodules	2 (1.4)
Left lung hypoplasia	1 (0.7)
Thyroid nodule or enlargement	3 (2.1)
Complex renal cyst	2 (1.4)
Liver and pancreatic significant siderosis	1 (0.7)
Liver lesion or cyst	8 (5.6)
Liver metastasis and splenic infarct	1 (0.7)
Total	19 (13.3)

Late gadolinium enhancement

A total of 120 patients (84.5%) underwent delayed gadolinium enhancement imaging. More than one-third of patients (n=45, 37.5%) had evidence of late-gadolinium enhancement. The distribution of scar volume quantification of the total LV included 18.3% with scar 1-5%, 5.8% with scar 6-10%, and 10.8% with scar >10% (*Table 1*). There were 9/45 patients (20%) that had scar in an ischemic distribution, one patient with scar in both ischemic and non-ischemic pattern, and with the remaining patients (78%) having scar in non-coronary artery disease territory.

Extra-cardiac incidental findings

A total of 19 (13.3%) extra-cardiac findings were identified and summarized in *Table 4*. One of the incidental findings (liver metastasis and splenic infarct) was previously known to the reader and prior identified on an abdominal computed tomography study, while the remaining 18 findings were not previously known.

Discussion

Cardiovascular imaging is a mainstay of contemporary practice, and plays a valuable role in the clinical management and guiding therapy of patients. The rapid evolution of technology with enhanced clinical application has promoted the growth of cardiac imaging. CMR for example provides several advantages to echocardiography particularly when there is a clinical need to assess and quantify the presence of scar, differentiate types of cardiomyopathy, RV quantification, provide tissue characterization, anatomic definition when echocardiography is limited by poor acoustic window, complex congenital cases with 3D volume reconstruction, and several others. However, there has been a parallel growth and fear of over-utilization, inappropriate testing, and the subsequent cost burden on third-party payers, patients and society. Hence, through the development of guidelines and appropriateness criteria, physicians have directed their efforts to eliminate unnecessary testing, and promote cost-conscious utilization of imaging and resources (17).

In the current retrospective analysis of all CMR studies performed at our institution since the inception of the program, 8.4% of the studies were not appropriate and did not yield relevant clinical information beyond what was known or suspected. Of the appropriate studies, CMR changed the diagnosis in one-third of cases, detected new pathology in 8% of cases, and showed important extra-cardiac findings in 9% of studies. One of the main strength of the paper is that it shows that one-third had an incorrect diagnosis prior to CMR. This is perhaps not unique to the Middle East or our institution, and had there been more cases, then many more patients would have benefited from this important technology. This brings out the issue of underutilization. This technology that has been present since 1990's has only started making its way in Lebanon.

This is the first study to our knowledge that evaluates appropriate CMR testing in accordance to recently published and revised guidelines. There have been several studies assessing appropriateness of other non-invasive testing in the region. For cardiac computed tomography (CCT), for example, El Sibai *et al.* showed improvement in the appropriate utilization of CCT from 8% in 2006 to 38% in 2010 at the same institution in Lebanon (18). In addition, Gholamrezanezhad *et al.* showed a 72.5% appropriate utilization of single photon emission computed tomography myocardial perfusion imaging in Iran in 2011 (19). Similarly, Gibbons *et al.* showed a 64% appropriate indication for stress nuclear imaging and stress echocardiography in the United States in 2008 (20). Gibbons *et al.* showed that adopting the guidelines results in improvement of appropriate testing with time (21).

The relatively high appropriate utilization of CMR studies at our institution is likely related to several factors. First, the referring physician most often contacted one of the imaging cardiologists or radiologists to discuss the case and the question in mind that the CMR study is supposed to answer before sending the patient for the study. In the

era of multimodality imaging, identifying which modality is the best to answer the question posed is recognized as part of the guidance duties of the cardiovascular imaging specialists (17). This is in the best interest of the patient to reduce unnecessary testing and hazardous exposures. Furthermore, given the worldwide observed increase in the cost incurred by the healthcare system to imaging in general, such practice, and not an unhealthy inter-modality specialists' competition, is foreseen as the best way to address cost increase concerns (17).

Second, as part of maintaining quality assurance, both cardiologists (Wael AlJaroudi and Hussain Isma'eel) randomly reviewed every other month few cases that were performed and interpreted by the other physician for appropriate indications and result interpretations. While this may not have impacted directly the results of this manuscript (given that all requests were performed and analyzed), it might have had a future impact on subsequent ordered studies and perhaps indirectly biased or discourage us against ordering such un-indicated studies. In the Middle East, assessment of appropriate indication as a quality metric is not widely practiced nor properly publicized, with certain factors leading to unwillingness to report (22). The healthcare administrative environment is not at a similar stage as their counterparts in the USA and Europe (23,24). Some insurance companies, however, do have a pre-approval requirement for certain studies, as is the case with CMR. These impose stringent criteria for approval, something not practiced with echocardiography, probably because CMR is being newly introduced and is more costly. However, even within the more affluent Gulf states in the region, healthcare cost constitutes a significant proportion of the national gross domestic product and is on the rise (Data from the World Bank: http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS), and therefore appropriate utilization assessment is bound to become more widely implemented soon.

Third, the CMR appropriateness criteria have been available and well known since 2006 and as the authors have experience in CMR for many years as part of their training abroad, this could have contributed to the high appropriate utilization rate. This in turn highlights the advantages of having healthcare professional societies (Society of CMR, Society of CCT, European Society of Cardiology, European Association of Cardiovascular Imaging, American Heart Association, American College of Cardiology, and others) being at the forefront of setting appropriateness criteria before insurance companies and government do that for us; and suggests that an earlier formal introduction of these concepts into the training of physicians might be useful in a changing healthcare environment.

Limitations

We recognize several limitations of the study. First, this is a retrospective study from a single tertiary referral center. We analyzed all patients including the first one since the initiation of the CMR program to minimize any potential selection bias. In addition, the evaluation of coronary artery disease and ischemia using stress testing CMR is not yet available at our institution. Hence, there were several potential appropriateness indications for the detection coronary artery disease, risk stratification, and preoperative evaluation that could not be evaluated, and therefore skewed our results. In the next few months, we will be launching stress CMR and we should be able to evaluate the appropriateness of these studies in the coming few years. Furthermore, we did not have any follow-up data to document impact on clinical management or outcome. We are currently preparing to build a prospective database with follow-up data. Finally, most of the referrals were internal and from cardiologists. Still, this manuscript represents one of the first experiences of a tertiary center in Lebanon and the region, and reflects an unbiased view of our population.

Future directions

With the expansion of the CMR program and introduction of stress CMR, cardio-oncology and hematology program, and adult congenital heart disease, we expect a steady increase in volume and widening of the types of studies and indications. It is imperative to continue to perform appropriate CMR studies when indicated, and minimize unnecessary tests particularly given the cost and financial burden on the society. Furthermore, it is important to build a prospective database with clinical follow-up, which is work in progress.

Conclusions

Despite the recent launch of the CMR program at our institution, the majority of studies were appropriately indicated, provided relevant data and were clinically useful. Inappropriate or uncertain studies did not provide relevant data beyond what was known or expected, and should be minimized to avoid unnecessary costs. Large prospective

CMR database with clinical follow-up is needed to provide more insight about cardiovascular disease and outcomes in our population.

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