Prior Authorization Review
Panel MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
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**Type of Submission – Check all that apply:**
- [ ] New Policy
- [x] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

**CPB 520 Magnetic Resonance Imaging of the Cardiovascular System - Cardiac MRI**

Clinical content was last revised on 05/24/2018. Additional non-clinical updates were made by Corporate since the last PARP submission, as documented below.

**Revision and Update History since last PARP submission:**
- 03/16/2018 - This CPB has been updated with additional coding.
- 05/24/2018 - This CPB has been revised to state that magnetic resonance imaging (MRI) of the cardiovascular system is considered medically necessary for detection of left atrial/left atrial appendage thrombus in persons with atrial fibrillation when echocardiogram is inconclusive.
- 05/23/2019 – Tentative next scheduled review date by Corporate.

Name of Authorized Individual (Please type or print):

Dr. Bernard Lewin, M.D.

Signature of Authorized Individual:

[Signature]

www.aetnabetterhealth.com/pennsylvania  Updated 03/16/2018
Magnetic Resonance Imaging of the Cardiovascular System - Cardiac MRI

Number: 0520

Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Policy

I. Medically Necessary Indications

Aetna considers magnetic resonance imaging (MRI) of the cardiovascular system medically necessary for the indications listed below, in accordance with guidelines developed by the American College of Cardiology Foundation, American College of Radiology (ACR) and the American Heart Association (AHA):

A. Thoracic aortic disease

For example: abnormal aortic contour or size on chest X-ray, differentiation of mediastinal mass versus vascular abnormality, to rule out aortic dissection, aneurysm, leaking thoracic aneurysm, exclude aortic source of peripheral embolization, Sinus Valsalva aneurysm, Marfan's syndrome and aorta annular ectasia, after therapy of aortic dissection of aortic arch anomalies, coarctation, following aortic angioplasty, periaortic abscess or infection; or
B. Pericardial disease

For example: to assess pericardial thickness and detection of metastases, for diagnosing pericardial cysts, pericarditis and constriction, for diagnosing effusion and tamponade; or

C. External or internal masses, pathology of lung and pleura

For example: chest wall and mediastinal tumor invasion of the lung and pleura, masses (e.g., lipoma), intracavity tumors, and differentiation of tumor from thrombus, assessment of vascular invasion, hilar assessment, and pericardial/myocardial invasion, pleural diseases; or

D. Pathology involving surrounding structures

For example: to evaluate intrinsic abnormalities of the pulmonary arteries, including central thrombi, aneurysms, stenoses, occlusions, dissection, and extra-vascular disease involving the pulmonary arteries; or

E. Assessment of right ventricular cardiomyopathy/dysplasia; or

F. Congenital heart disease

For example: ventricular septal defect, atrial septal defect, tetralogy of Fallot, transposition of the great arteries, pulmonary atresia, obstruction to the right ventricular outflow tract, other complex cyanotic heart disease, pulmonary venous anomalies, after surgery for correction of congenital heart disease; or

G. Cardiac function, morphology, and structure when the following criterion is met:

- After it has been determined that echocardiogram is inconclusive or expected to be non-diagnostic; or
H. Atrial fibrillation, for assessing left atrial structure and function, for
detecting thrombi in the left atrial appendage when echocardiogram is
inconclusive, and for identifying pulmonary vein anatomy prior to or after
electrophysiology procedures.

I. Diseases of the large veins

For example: acquired and congenital abnormalities of the superior or
inferior vena cavae, pulmonary vein system, or portal venous system
(e.g., vena caval thrombus, differentiation of tumor thrombus and blood
clot of the vena cava, superior vena caval syndrome, superior vena caval
invasion or encasement by lung or mediastinal tumors, diagnosis of
Budd-Chiari syndrome, and diagnosis of other caval anomalies); or

J. Valvular heart disease when the following criterion is met:

• After it has been determined that echocardiogram and Doppler
  studies are inconclusive or expected to be nondiagnostic; or

K. Coronary artery disease - Detection and localization of inducible
  myocardial perfusion deficits or inducible contractile dysfunction;
detection or quantification of the extent of acute or chronic myocardial
infarction; differentiation of recent from remote myocardial infarction.

L. Demonstration of complications of infarction - for example: formation of
  an aneurysm, mural thrombus formation, to demonstrate regional wall
  motion or wall thickening abnormalities of a damaged left ventricle.

M. Peripheral arterial disease (PAD)

To diagnose anatomical location and degree of stenosis of PAD and to
select individuals with lower extremity PAD as candidates for
endovascular intervention.

N. Cardiomyopathy
To evaluate cardiomyopathies (dilated, restrictive (amyloid), other infiltrative [sarcoid, Fabry, myocardial involvement in systemic myopathies], hypertrophic cardiomyopathy, or due to cardiotoxic therapies).

O. Myocarditis

For further evaluation of suspected acute or chronically active myocarditis

P. Children with suspected or confirmed pulmonary hypertension/pediatric pulmonary hypertensive vascular disease

As part of the diagnostic evaluation and during follow-up to assess changes in ventricular function and chamber dimensions.

II. Screening

Aetna considers MRI of the cardiovascular system experimental and investigational as a screening test for cardiovascular disease, for acute rejection following heart transplantation, for predicting ventricular tachyarrhythmic events (e.g., sudden cardiac death, resuscitated cardiac arrest, the occurrence of ventricular arrhythmias, and appropriate implantable cardioverter defibrillator therapy), and for all other indications (except for the ones listed above).

III. Intravascular MRI

Aetna considers intravascular MRI experimental and investigational for detecting coronary vulnerable plaques.

IV. Whole-Heart Coronary MRI

Aetna considers whole-heart coronary MRI experimental and investigational for the non-invasive evaluation of the coronary arteries.
V. Blood Oxgenation Level-Dependent Cardiac MRI

Aetna considers blood oxygenation level-dependent cardiac MRI experimental and investigational for assessing perfusion in individuals with critical limb ischemia because the effectiveness of this approach has not been established.

Requests for cardiac MRI for indications that are not listed above are subject to medical review.

Any evidence of duplicative services, such as the use of computerized axial tomography (CT) scan, radionuclide studies, ultrasound, radioisotope scanning, sonograms and MRI, is subject to medical review for an evaluation of the medical necessity of the MRI. There must be a compelling reason for multiple diagnostic procedures; in such situations, the MRI will only be considered medically necessary if the physician documents specific, necessary information to be gained from the additional test(s) that the initial test did not provide. If a claim reveals that MRI was performed to detect a suspected medically necessary indication but instead demonstrated a non-medically necessary indication, the MRI will be considered medically necessary.

Background

Magnetic resonance imaging (MRI) is a non-invasive imaging procedure used primarily for studying intra-cranial and intra-spinal pathology, and for evaluating abnormalities of the musculoskeletal system, the heart, and pelvis. It is also used to evaluate abdominal visceral problems.

Magnetic resonance imaging uses a pulsed radiofrequency wave in the presence of a high magnetic field to produce high quality images of the body in any plane. Magnetic resonance imaging may be preferred to a computed tomography (CT) scan because of its established capability to depict soft tissue, lack of radiation, and often without the need for contrast material.

During an MRI examination, the patient is placed inside a very strong magnet. A fraction of the hydrogen atoms within the patient's body align themselves with the magnetic field. The body area being examined is exposed to radio waves that are first absorbed and then emitted. The emitted waves become the MRI signal. The
signal is analyzed by computer and processed into images of the body. The images are usually in the form of slices through the body. The slices can be taken in any plane. Magnetic resonance imaging also has the ability to acquire 2-, 3- or 4-dimensional data. The signal intensity of a tissue in MRI images depends on the molecular environment of the protons. MRI parameter settings can be tuned to "highlight" certain tissues, e.g. make fat, water or other tissue appear particularly bright, or dark. Structures without proteins (air, calcium) always appear black. The novel technique of mapping uses signal intensity measurements of several images to estimate relaxation times. These have normal ranges and thus are less sensitive to subjective errors. Furthermore, mapping allows for detecting global myocardial abnormalities such as edema or an increased extracellular space.

Magnetic resonance imaging is sometimes performed with the use of contrast agents for specific indications in order to specifically modify the contrast in regions with increased or decreased contrast uptake. MRI contrast agents typically are based on gadolinium, which shorten relaxation times and thereby modify the signal in images. Typically, T1-weighted images are used for contrast-enhanced MRI scans. Contrast enhancement agents are approved by the Federal Drug Administration for use with MRI: Magnevist, (gadopentetate dimeglumine), ProHance, (gadoteritol), Omniscan, (gadodiomode), Ultravist, (iopromide), and Ferumoxsil (feroxide).

Magnetic resonance imaging has been shown to have several technical advantages in comparison to other standard diagnostic testing procedures such as CT scan and X-ray. Magnetic resonance imaging is a non-invasive technique that uses no ionizing radiation and according to available literature, there are no known clinically significant side effects. The literature indicates that MRI can be used during the first trimester of pregnancy when it has been shown to offer an advantage over other modalities. Magnetic resonance imaging does not always require contrast agents in order to achieve a high degree of resolution. The literature indicates there is some increased risk of administering MRI contrast agents to patients with asthma or iodine allergy, but administration of these agents is still performed with caution. Magnetic resonance imaging soft tissue contrast has been shown to be superior to that of other imaging modalities, and there are no image artifacts from bone. The literature indicates MRI has greater inherent contrast between different types of normal body tissues and between pathological tissues and normal tissues. Magnetic resonance
imaging clarity is equal in any view: axial, sagittal, coronal, or oblique. Magnetic resonance imaging also has the ability to acquire 2-dimensional, 3-dimensional and 4-dimensional data.

Magnetic resonance imaging has been shown to have several disadvantages. It requires more patient cooperation than other tests. Imaging time is longer than CT or X-ray. For MRI, the acquisition time per image is similar to the time required for a CT slice (current minimal acquisition times 34ms for MRI and 65ms for dual-source CT), while the temporal resolution can be increased by repeated measurements to less than 20ms. It has limitations in the acute trauma setting due to its incompatibility with various medical and life support devices. Overheating may result from the alternating magnetic transmissions of the radiofrequency coils. The literature indicates that care should be exercised when using MRI with infants, elderly patients, and hyperpyrexic individuals (NIH, 1987). There is a forceful attraction of ferromagnetic objects to the magnet. Most aneurysm clips, intra-cranial or intra-ocular metal, shrapnel, cardiac pacemakers or pacemaker wires and cochlear implants are absolute contraindications for MRI. Magnetic resonance imaging has somewhat less spatial resolution than CT scan.

Magnetic resonance imaging in the field of cardiology is evolving at a dynamic pace. However, because of the lack of availability of state of the art MRI technology and expertise, echocardiography, in particular trans-esophageal echocardiogram (TEE), remains the generally accepted modality for the evaluation of cardiac anatomy and function most of the time by most practitioners. According to the literature, 50 to 60 % of the population can not be adequately imaged with echocardiogram. For these patients, MRI has been shown to be particularly important. Magnetic resonance imaging has the following important attributes that make it effective for the evaluation of the cardiovascular system:

- Fast gradient echo techniques can be used to assess global and regional ventricular contractile function;
- It can produce high resolution images of the cardiac chambers and large vessels without the need of contrast agents;
- It does not have difficulties in evaluating right ventricular function;
- It does not have the weakness of geometric assumptions as does angiography and echocardiography in the assessment of ventricular volumes;
- It has high tissue contrast;
- It is a 3-dimensional imaging technique;
- It produces images of cardiovascular structures without the interference from adjacent bone or air; and
- Velocity encoded techniques permit measurement of blood flow.

Since MRI can usually not be brought to the bedside like the TEE, it may not be the first test used in an emergency situation, but may be used to better define the diagnosis. Under established guidelines, MRI is used as the diagnostic test for the following indications: diseases of the aorta, diseases of the pericardium, external and internal masses, pathology involving surrounding structures, congenital heart disease, and ventricular dysplasia. Magnetic resonance imaging is increasingly being used in the assessment of cardiac function, morphology and structure. When echocardiography does not provide enough information, in these circumstances, the literature suggests MRI may be warranted.

García-García et al (2008) noted that thin-capped fibroatheroma is the morphology that most resembles plaque rupture. Detection of these vulnerable plaques is essential for studying their natural history and assessing potential therapies and, thus, may have an important impact on the prevention of myocardial infarction and death. At the present time, conventional grayscale intra-vascular ultrasound, virtual histology and palpography data are being collected with the same catheter during the same pullback. A combination of this catheter with either thermography capability or additional imaging, such as optical coherence tomography or spectroscopy, would be an exciting development. Intra-vascular MRI also holds much promise. To date, none of the techniques described above has been sufficiently validated and, most importantly, their predictive value for adverse cardiac events remains elusive. Very rigorous and well-designed studies are compelling for defining the role of each diagnostic modality. Until vulnerable plaques can be detected accurately, no specific treatment is warranted.

Hauser and Manning (2008) stated that the non-invasive detection of coronary artery disease has been a major goal of newer cardiac imaging technologies. In the past 10 years, coronary MRI has undergone significant advances, resulting in excellent sensitivity for detecting coronary artery disease. The authors noted that whole-heart coronary MRI, a technique that is similar to coronary CT angiography, has emerged as a promising approach for the non-invasive evaluation of the coronary arteries. This is in agreement with the observation of Schaar et al (2007) who noted that the role of non-invasive imaging in vulnerable plaque detection is currently under investigation. Several invasive and non-invasive techniques (e.g., MRI and multi-
slice spiral CT) are currently under development to evaluate the vulnerable plaque. However, none has proven its value in an extensive in-vivo validation and all have a lack of prospective data.

In a review on the use of cardiac MRI in the diagnosis of acute coronary syndrome (ACS), Breuckmann et al (2008) noted that in contrast to chronic myocardial infarction, data concerning the value of cardiac MRI in patients with acute onset of chest pain are still rare. Even in the presence of characteristic clinical parameters, cardiac MRI might provide independent evidence especially in the absence of typical ECG alterations and prior to biomarker elevation. Besides the ability to demonstrate wall motion abnormalities, cardiac MRI gains additional potential as to the detection of myocardial edema, microvascular obstruction (no-reflow) and myocardial necrosis. However, cardiac MRI is expensive and time-consuming, and thus may not be cost-effective. Currently, a lack of sufficient diagnostic and prognostic data would make cardiac MRI unsuitable for routine stratification of chest pain patients in an emergency department.

Lockie and colleagues (2009) stated that the role of cardiac MRI in the assessment of ACS is less well-established. Future larger studies will determine more fully the role of cardiac MRI in the setting of ACS. The American College of Radiology's Expert Panel on Cardiac Imaging (Hoffman et al, 2011) rendered a "2" rating for MRI of heart with or without stress without contrast; and a "3" rating for MRI of heart with or without stress without and with contrast for evaluation of patients with acute non-specific chest pain (rating Scale: 1,2,3 means "usually not appropriate"; 4,5,6 means "may be appropriate"; and 7,8,9 means "usually appropriate").

A report of the American College of Cardiology Foundation task force on cardiovascular magnetic resonance (Hundley et al, 2010) stated that cardiovascular MRI (performed with gandolinium enhancement) is recommended to diagnose anatomical location and degree of stenosis of peripheral arterial disease (PAD) and to select patients with lower extremity PAD as candidates for endovascular intervention.

The ACC report stated that cardiac MRI may be used for assessing left atrial structure and function in patients with atrial fibrillation, and may be useful for identifying pulmonary vein anatomy prior to or after electrophysiology procedures without need for patient exposure to ionizing radiation. The report also noted that
standardization of protocols and more studies are needed to ascertain whether cardiovascular MRI provides a reliable method for detecting thrombi in the left atrial appendage in patients with atrial fibrillation.

An UpToDate review on “Ventricular septal defect in adults” (Ammash and Connolly, 2013) states that “Cardiovascular magnetic resonance (CMR) imaging and computed tomography (CT) can provide accurate, reliable and reproducible assessment of cardiac structure and function in congenital heart disease when performed by an expert. These techniques offer certain advantages over echocardiography since they allow unrestricted evaluation of cardiac chambers and great arteries not compromised by air, bone, or surgical scar. Summation of disks on multiple tomographic slices during ventricular diastole and systole permits direct and accurate measurement of left ventricular volume and function. Such data is helpful in timing intervention or repair in adults with VSDs. However, these techniques have not been widely adopted in the evaluation of VSD primarily because echocardiography is widely available and provides sufficient information in most cases and CMR and cardiac CT have more limited availability”.

MedlinePlus, a service of the U.S. National Library of Medicine, notes that cardiac MRI is one of the tests that are used for evaluation of VSD. The Adult Congenital Heart Association (ACHA) states that tests to confirm the presence and effect of a VSD may include cardiac MRI.

In an eMedicine review on “Ventricular septal defects”, Ramaswamy (2013) states that “MRI is a useful adjunct tool, but it is infrequently required for the diagnosis of VSDs. As a rule, it is employed only when ultrasonography is not feasible or when ultrasonographic findings are not diagnostic. However, because MRI data about systemic and pulmonary flows are been well-validated and well-correlated with catheterization data, one of the indications for the use of MRI is evaluation of a VSD that is judged to be borderline during echocardiography in terms of the level of the left-to-right shunt. For such defects, an MRI-derived Qp:Qs may assist the clinician in making the decision whether to proceed with surgical treatment.

Sarcoidosis and amyloidosis are both multi-system disorders, which may involve the heart; however, isolated cardiac disease is rare. Diagnosis of cardiac sarcoidosis and amyloidosis is crucial because the patient prognosis is dependent on cardiac involvement and early treatment. Bauner and Wintersperger (2013) stated that echocardiography is the first line imaging modality in the diagnostic work-up of both
diseases, possibly giving hints towards the correct diagnosis. Besides myocardial biopsy and radionuclide studies cardiac MRI is routinely performed in patients suspect of having infiltrative cardiomyopathy. The T1 mapping procedure is currently being evaluated as a new technique for detection and quantification of global myocardial enhancement, as seen in cardiac amyloidosis. Sensitivities and specificities for detection of cardiac sarcoidosis and amyloidosis can be significantly improved by MRI, especially with late gadolinium enhancement (LGE) imaging. In cardiac sarcoidosis the use of LGE is outcome-related while in amyloidosis analysis of T1-mapping may be of prognostic value. The authors recommended that if cardiac involvement in sarcoidosis or amyloidosis is suspected cardiac MRI including LGE should be performed for establishing the diagnosis.

An UpToDate review on “Cardiac sarcoidosis” (McKenna, 2013) states that “In patients with abnormalities after the initial evaluation, we suggest noninvasive imaging, preferably with cardiovascular magnetic resonance imaging (CMR) and FDG PET to enhance disease detection and monitoring of treatment response. If neither CMR nor PET is available, we suggest a gallium, thallium, or technetium scan”.

Maron (2012) stated that hypertrophic cardiomyopathy (HCM) is characterized by substantial genetic and phenotypic heterogeneity, leading to considerable diversity in clinical course including the most common cause of sudden cardiac death (SCD) in young people and a determinant of heart failure symptoms in patients of any age. Traditionally, 2-dimensional echocardiography has been the most reliable method for establishing a clinical diagnosis of HCM. However, cardiovascular magnetic resonance (CMR), with its high spatial resolution and tomographic imaging capability, has emerged as a technique particularly well-suited to characterize the diverse phenotypic expression of this complex disease. For example, CMR is often superior to echocardiography for HCM diagnosis, by identifying areas of segmental hypertrophy (i.e., anterolateral wall or apex) not reliably visualized by echocardiography (or under-estimated in terms of extent). High-risk HCM patient subgroups identified with CMR include those with thin-walled scarred left ventricular (LV) apical aneurysms (which prior to CMR imaging in HCM remained largely undetected), end-stage systolic dysfunction, and massive LV hypertrophy. Cardiovascular magnetic resonance observations also suggested that the cardiomyopathic process in HCM is more diffuse than previously regarded, extending beyond the LV myocardium to include thickening of the right ventricular wall as well as substantial morphologic diversity with regard to papillary muscles and
mitral valve. These findings have implications for management strategies in patients undergoing invasive septal reduction therapy. Among HCM family members, CMR has identified unique phenotypic markers of affected genetic status in the absence of LV hypertrophy including: myocardial crypts, elongated mitral valve leaflets and late gadolinium enhancement (LGE). The unique capability of contrast-enhanced LGE-CMR to identify myocardial fibrosis has raised the expectation that this may represent a novel marker, which may enhance risk-stratification. At this time, LGE appears to be an important determinant of adverse LV re-modeling associated with systolic dysfunction. However, the predictive significance of LGE for SCD is incompletely resolved and ultimately future large prospective studies may provide greater insights into this issue.

Green et al (2012) performed a systematic review and meta-analysis of the predictive value of LGE-CMR for future cardiovascular events and death in patients with HCM. These investigators searched multiple databases including PubMed for studies of LGE in HCM that reported selected clinical outcomes (cardiovascular mortality, SCD, aborted SCD, and heart failure death). They performed a systematic review of the literature and meta-analysis to determine pooled odds ratios for these clinical events. A total of 4 studies evaluated 1,063 patients over an average follow-up of 3.1 years. The pooled prevalence of LGE was 60 %. The pooled odds ratios (OR) demonstrated that LGE-CMR correlated with cardiac death (pooled OR: 2.92, 95 % confidence interval [CI]: 1.01 to 8.42; p = 0.047), heart failure death (pooled OR: 5.68, 95 % CI: 1.04 to 31.07; p = 0.045), and all-cause mortality (pooled OR: 4.46, 95 % CI: 1.53 to 13.01; p = 0.006), and showed a trend toward significance for predicting sudden death/aborted sudden death (pooled OR: 2.39, 95 % CI: 0.87 to 6.58; p = 0.091). The authors concluded that LGE-CMR has prognostic value in predicting adverse cardiovascular events among HCM patients. There are significant relationships between LGE and cardiovascular mortality, heart failure death, and all-cause mortality in HCM. Additionally, LGE and SCD/aborted SCD displayed a trend toward significance. They stated that assessment of LGE-CMR has the potential to provide important information to improve risk-stratification in HCM in clinical practice.

Gulati et al (2013) examined if myocardial fibrosis (detected by LGE-CMR imaging) is an independent and incremental predictor of mortality and SCD in dilated cardiomyopathy. Prospective, longitudinal study of 472 patients with dilated cardiomyopathy referred to a United Kingdom center for CMR imaging between November 2000 and December 2008 after presence and extent of mid-wall...
replacement fibrosis were determined. Patients were followed-up through December 2011. Primary end point was all-cause mortality. Secondary end points included cardiovascular mortality or cardiac transplantation; an arrhythmic composite of SCD or aborted SCD (appropriate ICD shock, non-fatal ventricular fibrillation, or sustained ventricular tachycardia); and a composite of heart failure (HF) death, HF hospitalization, or cardiac transplantation. Among the 142 patients with mid-wall fibrosis, there were 38 deaths (26.8 %) versus 35 deaths (10.6 %) among the 330 patients without fibrosis (hazard ratio [HR], 2.96 [95 % CI: 1.87 to 4.69]; absolute risk difference, 16.2 % [95 % CI: 8.2 % to 24.2 %]; p < 0.001) during a median follow-up of 5.3 years (2,557 patient-years of follow-up). The arrhythmic composite was reached by 42 patients with fibrosis (29.6 %) and 23 patients without fibrosis (7.0 %) (HR, 5.24 [95 % CI: 3.15 to 8.72]; absolute risk difference, 22.6 % [95 % CI: 14.6 % to 30.6 %]; p < 0.001). After adjustment for left ventricular ejection fraction (LVEF) and other conventional prognostic factors, both the presence of fibrosis (HR, 2.43 [95 % CI: 1.50 to 3.92]; p < 0.001) and the extent (HR, 1.11 [95 % CI: 1.06 to 1.16]; p < .001) were independently and incrementally associated with all-cause mortality. Fibrosis was also independently associated with cardiovascular mortality or cardiac transplantation (by fibrosis presence: HR, 3.22 [95 % CI: 1.95 to 5.31], p < 0.001; and by fibrosis extent: HR, 1.15 [95 % CI: 1.10 to 1.20], p < 0.001), SCD or aborted SCD (by fibrosis presence: HR, 4.61 [95 % CI: 2.75 to 7.74], p < 0.001; and by fibrosis extent: HR, 1.10 [95 % CI: 1.05 to 1.16], p < 0.001), and the HF composite (by fibrosis presence: HR, 1.62 [95 % CI: 1.00 to 2.61], p = 0.049; and by fibrosis extent: HR, 1.08 [95 % CI: 1.04 to 1.13], p < 0.001). Addition of fibrosis to LVEF significantly improved risk re-classification for all-cause mortality and the SCD composite (net re-classification improvement: 0.26 [95 % CI: 0.11 to 0.41]; p = 0.001 and 0.29 [95 % CI: 0.11 to 0.48]; p = 0.002, respectively). The authors concluded that assessment of mid-wall fibrosis with LGE-CMR imaging provided independent prognostic information beyond LVEF in patients with non-ischemic dilated cardiomyopathy. They stated that the role of LGE-CMR in the risk-stratification of dilated cardiomyopathy requires further investigation.

Scott et al (2013) noted that approaches to the risk-stratification for SCD remain unsatisfactory. Although LGE-CMR for SCD risk-stratification has been evaluated in several studies, small sample size has limited their clinical validity. These investigators performed a meta-analysis to better-gauge the predictive accuracy of LGE-CMR for SCD risk-stratification. Electronic databases and published bibliographies were systematically searched to identify studies evaluating the association between the extent of LV scar on LGE-CMR and ventricular arrhythmic
events [SCD, resuscitated cardiac arrest, the occurrence of ventricular arrhythmias, or appropriate implantable cardioverter defibrillator (ICD) therapy]. Only studies enrolling patients with CAD or non-ischemic cardiomyopathy were included. Summary estimates of the relative risk (RR) and likelihood ratios (LRs) were calculated using random effects models. A total of 11 studies comprising 1,105 patients were identified. During a mean/median follow-up of 8.5 to 41 months 207 patients had ventricular arrhythmic events. Ventricular arrhythmic events were more common in patients with a greater extent of LV scar: RR 4.33 [95 % CI: 2.98 to 6.29], positive LR 1.98 (95 % CI: 1.66 to 2.37), and negative LR 0.33 (95 % CI: 0.24 to 0.46). The authors concluded that the extent of LGE on CMR is strongly associated with the occurrence of ventricular arrhythmias in patients with reduced left ventricular ejection fraction and may be a valuable risk-stratification tool for identifying patients who will benefit from ICD therapy. However, they stated that uncertainties regarding clinical application persist and need to be addressed prior to introduction into broad clinical practice.

den Hartog et al (2013) provided an overview of the literature that assessed the agreement between MRI and histology for specific carotid plaque characteristics associated with vulnerability in terms of sensitivity and specificity. A systematic search strategy was conducted in MEDLINE and EMBASE databases resulting in 1,084 articles; these investigators included 17 papers. Due to variation in presentation, especially in MRI and histology methods, a pooled analysis could not be performed. Two studies were performed on a 3.0-T MRI scanner; all other studies were performed on a 1.5-T scanner. Most performed sequences were two-dimensional (2-D) and 3-D T1-weighted and all histology protocols varied slightly. These findings indicated that calcification, fibrous cap, intra-plaque hemorrhage (IPH) and lipid-rich necrotic cores can be identified with moderate-to-good sensitivity and specificity. The authors concluded that based on current literature, it appears premature for routine application of MRI as an imaging modality to assess carotid plaque characteristics associated with plaque vulnerability. They stated that although MRI still holds promise, clinical application for plaque characterization would require consensus regarding MRI settings and confirmation by histology. Pre-defined protocols for histology and MR imaging need to be established.

Saam et al (2013) performed a systematic review and meta-analysis to determine precise estimates of the predictive value of carotid IPH as determined by MRI for cerebrovascular events. These investigator searched PubMed, EMBASE, and the Cochrane Library through September 2012 for studies that followed more than 35
individuals after baseline MRI. Independent observers abstracted information on populations, MR techniques, outcomes, and study quality. Risk estimates of the presence of IPH for cerebrovascular events were derived in random effects regression analysis, and causes of heterogeneity were determined in meta-regression analysis. These researchers identified 8 eligible studies including 689 participants who underwent carotid MRI. The prevalence of IPH at baseline was high (49.0 %). Over a median follow-up of 19.6 months, a total of 108 cerebrovascular events occurred (15.7 % event rate). The presence of IPH was associated with an approximately 6-fold higher risk for events (HR: 5.69; 95 % CI: 2.98 to 10.87). The annualized event rate in subjects with detectable IPH was 17.71 % compared with 2.43 % in patients without IPH. Meta-regression analysis showed symptomatic subjects had higher risks as compared with asymptomatic subjects (HR: 11.71, 95 % CI: 5.17 to 26.48 versus HR: 3.50, 95 % CI: 2.59 to 4.73, p = 0.0065). Also, differences were observed for sex and sample size (all p < 0.01), with moderate visual publication bias due to missing smaller sample-size studies (p = 0.18). The authors concluded that presence of IPH on MRI strongly predicts cerebrovascular events. Moreover, they stated that homogenization of future studies is needed to allow for sufficient assessment of level of evidence for intervention trials.

**Graft Monitoring Following Heart Transplantation:**

International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients (Costanzo, et al., 2010) state that the routine clinical use of MRI for acute allograft rejection monitoring is not recommended. Furthermore, an UpToDate review on “Clinical utility of cardiovascular magnetic resonance imaging” (Fuisz and Pohost, 2015) does not mention cardiac rejection as a potential indication of CMR.

Usman et al (2012) noted that acute rejection is a major factor impacting survival in the first 12 months after cardiac transplantation. Transplant monitoring requires invasive techniques. Cardiac magnetic resonance (CMR) has been used in monitoring heart transplants. Prolonged T2 relaxation has been related to transplant edema and possibly rejection. These researchers hypothesized that prolonged T2 reflects transplant rejection and that quantitative T2 mapping will concur with the pathological and clinical findings of acute rejection. In a pilot study, patients were recruited within the 1st year after transplantation. Biopsies were graded according to the International Society for Heart Lung Transplant system for cellular rejection with immunohistochemistry for humoral rejection. Rejection was also considered if
patients presented with signs and symptoms of hemodynamic compromise without biopsy evidence of rejection who subsequently improved with treatment. Patients underwent a novel single-shot T2-prepared steady-state free precession 4-chamber and 3 short axis sequences and regions of interest were drawn overlying T2 maps by 2 independent blinded reviewers. A total of 74 (68 analyzable) CMRs T2 maps in 53 patients were performed. There were 4 cellular, 2 humoral, and 2 hemodynamic rejection cases. The average T2 relaxation time for grade 0R (n = 46) and grade 1R (n = 17) was 52.5 ± 2.2 and 53.1 ± 3.3 ms (mean ± SD), respectively. The average T2 relaxation for grade 2R (n = 3) was 59.6 ± 3.1 ms and 3R (n = 1) was 60.3 ms (all p value < 0.05 compared with controls). The T2 average in humoral rejection cases (n = 2) was 59.2 ± 3.3 ms and the hemodynamic rejection (n = 2) was 61.1 ± 1.8 ms (p < 0.05 versus controls). The average T2 relaxation time for all-cause rejection versus no rejection is 60.1 ± 2.1 versus 52.8 ± 2.7 ms (p < 0.05). All rejection cases were rescanned 2.5 months after treatment and demonstrated T2 normalization with average of 51.4 ± 1.6 ms. No difference was found in ventricular function between non-rejection and rejection patients, except in ventricular mass 107.8 ± 10.3 versus 127.5 ± 10.4 g (p < 0.05). The authors concluded that quantitative T2 mapping offered a novel non-invasive tool for transplant monitoring, and these initial findings suggested potential use in characterizing rejections. Given the limited numbers, a larger multi-institution study may help elucidate the benefits of T2 mapping as an adjunctive tool in routine monitoring of cardiac transplants.

Urbanowicz et al (2014) stated that diagnosis of rejection is a major objective in the management of heart transplant recipients. It has been reported that 1/3 of protocol biopsies in asymptomatic, biochemically stable organ transplant recipients in the first 6 months show unsuspected subclinical graft rejection. These researchers presented the case of a 43-year old man suffering from dilated cardiomyopathy who underwent orthotropic heart transplantation. The patient was admitted for a protocol endomyocardial biopsy and MRI on the 4th post-operative month as a protocol procedure. The examination revealed clinical status NYHA I with no signs of fatigue, diminution of exercise tolerance, or shortness of breath. His body temperature was not raised. He was referred for endomyocardial biopsy and cardiovascular magnetic resonance (CMR) imaging, which showed good left and right ventricle function and contractility. T2 imaging revealed increased signal in the area of the right ventricular free wall, seen both in 4-chamber and short axis views. The patient underwent an endomyocardial biopsy, which demonstrated diffuse infiltrate with multifocal miocyte damage and cellular edema recognized as acute rejection (3a ISHLT grade). Consequently, the patient was treated with parenteral methylprednisolone.
administration. The CMR study performed after 1 week of therapy showed that the signal intensity of the edematous areas was significantly decreased. Repetitive endomyocardial biopsy revealed no signs of rejection. The authors concluded that CMR can be helpful in graft monitoring following heart transplantation. It gives a whole-heart perspective that can be competitive with and/or complementary to endomyocardial biopsy.

**Diagnosis and Disease Monitoring of Cardiac Involvement in Systemic Amyloidosis:**

American College of Cardiology appropriate use criteria for cardiac MRI (2006) rated evaluation of specific cardiomyopathies (infiltrative [amyloid, sarcoid], HCM, or due to cardiotoxic therapies) as an appropriate indication for cardiac MRI.

Barison et al (2015) noted that cardiac involvement in systemic amyloidosis is caused by the extracellular deposition of misfolded proteins, mainly immunoglobulin light chains (AL) or transthyretin (ATTR), and may be detected by CMR. These researchers measured myocardial extra-cellular volume (ECV) in amyloid patients with a novel T1 mapping CMR technique and determined the correlation between ECV and disease severity. A total of 36 patients with biopsy-proven systemic amyloidosis (mean age of 70 ± 9 years, 31 men, 30 with AL and 6 with ATTR amyloidosis) and 7 patients with possible amyloidosis (mean age of 64 ± 10 years, 6 men) underwent comprehensive clinical and CMR assessment, with ECV estimation from pre- and post-contrast T1 mapping; 30 healthy subjects (mean age of 39 ± 17 years, 21 men) served as the control group. Amyloid patients presented with LV concentric hypertrophy with impaired bi-ventricular systolic function. Cardiac ECV was higher in amyloid patients (definite amyloidosis, 0.43 ± 0.12; possible amyloidosis, 0.34 ± 0.11) than in control subjects (0.26 ± 0.04, p < 0.05); even in amyloid patients without late gadolinium enhancement (0.35 ± 0.10), ECV was significantly higher than in the control group (p < 0.01). A cut-off value of myocardial ECV greater than 0.316, corresponding to the 95th percentile in normal subjects, showed a sensitivity of 79 % and specificity of 97 % for discriminating amyloid patients from control subjects (area under the curve of 0.884). Myocardial ECV was significantly correlated with LVEF (R(2) = 0.16), LV mean wall thickness (R(2) = 0.41), LV diastolic function (R(2) = 0.21), right ventricular ejection fraction (R(2) = 0.13), N-terminal fragment of the pro-brain natriuretic peptides (R(2) = 0.23) and cardiac troponin (R(2) = 0.33). The authors concluded that myocardial ECV was
increased in amyloid patients and correlated with disease severity. Thus, measurement of myocardial ECV represents a potential non-invasive index of amyloid burden for use in early diagnosis and disease monitoring.

**Detection of Subclinical Cardiac Involvement in Kearns-Sayre Syndrome:**

Kabunga et al (2015) stated that Kearns-Sayre syndrome (KSS) is a mitochondrial disorder characterized by onset before the age of 20 years, progressive external ophthalmoplegia, and pigmentary retinopathy, accompanied by cardiac conduction defects, elevated cerebrospinal fluid protein or cerebellar ataxia; 50% of patients with KSS develop cardiac complications. The most common cardiac manifestation is conduction disease that may progress to complete atrio-ventricular block or bradycardia-related polymorphic ventricular tachycardia (PMVT). The management of cardiac electrical disease associated with KSS and mitochondrial cytopathy was systematically reviewed including the case of a 23-year old female patient with KSS who developed a constellation of cardiac arrhythmias including rapidly progressive conduction system disease and monomorphic ventricular tachycardia with myocardial scarring. The emerging role of cardiac MRI (CMR) in detecting subclinical cardiac involvement was also highlighted.

An UpToDate review on “Mitochondrial myopathies: Clinical features and diagnosis" (Genge and Massie, 2105) states that “Kearns-Sayre syndrome (KSS) refers to the combination of CPEO [chronic progressive external ophthalmoplegia] with pigmentary retinopathy and onset before age 20. Other abnormalities have been described, including short stature, cerebellar ataxia, raised CSF protein (> 100 mg/dL), cardiac conduction defects or cognitive deficits/mental retardation. KSS is usually more aggressive than isolated CPEO, progressing to complete ophthalmoparesis, and often to death by the fourth decade due to the associated deficits. Patients with either disorder can develop a proximal myopathy, which usually does not limit daily functioning, particularly for patients with CPEO”. This review does not mention cardiac MRI as a management tool.

**Children with Suspected or Confirmed Pulmonary Hypertension/Pulmonary Hypertensive Vascular Disease:**

Qian and co-workers (2015) examined the clinical value of CMR imaging in the assessment of right ventricular (RV) function in patients with PH. The PubMed/Medline, Wanfang data, CNKI (from January 2001 to April 2015) were searched. The search terms were pulmonary arterial hypertension, right ventricular...
function, and cardiac magnetic resonance imaging. An inclusion criterion was patients suffering from PH, and healthy volunteers served as controls. All the subjects investigated had received CMR imaging. Main outcome measures included right ventricular end diastolic volume (RVEDV), right ventricular end systolic volume (RVESV) and right ventricular ejection fraction (RVEF). Meta-analysis was conducted by RevMan 5.0 software provided by Cochrane Collaboration, and the publication bias was analyzed by the funnel plot analysis. A total of 5 papers involving 381 patients met inclusion criteria. It was showed by meta-analysis that compared with healthy control group, RVEDV was increased in the PH group [weighted mean difference (WMD) = 33.96, 95% CI: 20.80 to 47.12, \( p < 0.00001 \)], RVESV was increased (WMD = 41.91, 95% CI: 29.63 to 54.19, \( p < 0.00001 \)), and RVEF was decreased (WMD = -20.09, 95% CI: -22.65 to -17.52, \( p < 0.00001 \)). The authors concluded that CMR imaging can be used to evaluate RV function of patients with PH, and it has important significance in the evaluation of RV function in patients with PH.

Baggen and associates (2016) provided a comprehensive overview of all reported CMR findings that predict clinical deterioration in PH. Medline and Embase electronic databases were systematically searched for longitudinal studies published by April 2015 that reported associations between CMR findings and adverse clinical outcome in PAH. Studies were appraised using previously developed criteria for prognostic studies. Meta-analysis using random effect models was performed for CMR findings investigated by 3 or more studies. A total of 8 papers (539 patients) investigating 21 different CMR findings were included. Meta-analysis showed that RVEF was the strongest predictor of mortality in PH (pooled HR 1.23 [95% CI: 1.07 to 1.41], \( p = 0.003 \)) per 5% decrease. In addition, RVEDV index (pooled HR 1.06 [95% CI: 1.00 to 1.12], \( p = 0.049 \)), RVESV index (pooled HR 1.05 [95% CI: 1.01 to 1.09], \( p = 0.013 \)) and LVEDV index (pooled HR 1.16 [95% CI: 1.00 to 1.34], \( p = 0.045 \)) were of prognostic importance; RV and LV mass did not provide prognostic information (\( p = 0.852 \) and \( p = 0.983 \), respectively). The authors concluded that the findings of this meta-analysis substantiated the clinical yield of specific CMR findings in the prognostication of PH patients. Decreased RV ejection was the strongest and most well established predictor of mortality. The authors stated that CMR is useful for prognostication in PH; RVEF was the strongest predictor of mortality. Moreover, they noted that serial CMR evaluation appeared to be of additional prognostic importance.
Latus and colleagues (2016) stated that childhood PH is a heterogeneous disease associated with considerable morbidity and mortality. Invasive assessment of hemodynamics is crucial for accurate diagnosis and guidance of medical therapy. However, adequate imaging is increasingly important in children with PH to evaluate the right heart and the pulmonary vasculature. Cardiac MRI and CT represent important non-invasive imaging modalities that may enable comprehensive assessment of RV function and pulmonary hemodynamics. These investigators presented graded consensus recommendations for the evaluation of children with PH by CMR and CT. They provided a structured approach for the use of CMR and CT imaging, emphasizing non-invasive variables of RV function, myocardial tissue and afterload parameters that may be useful for initial diagnosis and monitoring. The authors noted that the European Pediatric Pulmonary Vascular Disease Network, endorsed by the International Society of Heart and Lung Transplantation (ISHLT) and the German Society of Pediatric Cardiology (DGPK), recommended cardiac MRI, without anesthesia/sedation, for children with suspected or confirmed pulmonary hypertension/pediatric pulmonary hypertensive vascular disease as part of the diagnostic evaluation and during follow-up to assess changes in ventricular function and chamber dimensions (Class of Recommendation = 1; Level of Evidence = B).

Blood Oxygenation Level-Dependent Cardiac MRI in individuals with Critical Limb Ischemia:

Bajwa and colleagues (2016) noted that use of blood oxygenation level-dependent CMR (BOLD-CMR) to assess perfusion in the lower limb has been hampered by poor reproducibility and a failure to reliably detect post-revascularization improvements in patients with critical limb ischemia (CLI). These researchers developed BOLD-CMR as an objective, reliable clinical tool for measuring calf muscle perfusion in patients with CLI. The calf was imaged at 3-T in young healthy control subjects (n = 12), age-matched control subjects (n = 10), and patients with CLI (n = 34). Signal intensity time curves were generated for each muscle group and curve parameters, including signal reduction during ischemia (SRi) and gradient during reactive hyperemia (Grad). BOLD-CMR was used to assess changes in perfusion following revascularization in 12 CLI patients. Muscle biopsies (n = 28), obtained at the level of BOLD-CMR measurement and from healthy proximal muscle of patients undergoing lower limb amputation (n = 3), were analyzed for capillary-fiber ratio. There was good inter-user and inter-scan reproducibility for Grad and SRi (all p < 0.0001). The ischemic limb had lower Grad and SRi compared with the contralateral asymptomatic limb, age-matched control subjects, and young control...
subjects (p < 0.001 for all comparisons). Successful revascularization resulted in improvement in Grad (p < 0.0001) and SRi (p < 0.0005). There was a significant correlation between capillary-fiber ratio (p < 0.01) in muscle biopsies from amputated limbs and Grad measured pre-operatively at the corresponding level. The authors concluded that BOLD-CMR showed promise as a reliable tool for assessing perfusion in the lower limb musculature and merits further investigation in a clinical trial.

Detection of Left Atrial/Left Atrial Appendage Thrombus in Patients with Atrial Fibrillation:

In a meta-analysis, Chen and colleagues (2018) evaluated the accuracy of CMR in detecting left atrial/left atrial appendage (LA/LAA) thrombus and analyzed the difference between the diagnostic accuracy of various imaging sequences. PubMed, Web of Science, Embase, and the Cochrane Library were systematically searched for studies from 2000 to 2017 that compared CMR with transesophageal echocardiography (TEE) in detecting LA/LAA thrombus. The CMR images were analyzed in 4 categories: cine-CMR; first-pass contrast-enhanced 3D CMR angiography (CE-MRA); delayed-enhancement CMR (DE-CMR); and CMR, regardless of the magnetic resonance sequences used. Descriptive and quantitative information was extracted and Meta-DiSc 1.4 was used to perform the analysis. The analysis included 582 patients from 7 publications. The pooled sensitivity, specificity, diagnostic OR, LR+, LR-, and summary receiver operating characteristic (ROC) of cine-CMR were 91.00 %, 93.00 %, 50.43, 10.04, 0.24, and 93.93 %, respectively; for CE-MRA, the values were 77.00 %, 97.00 %, 179.21, 51.77, 0.30, and 97.63 %, respectively; for DE-CMR, 100.00 %, 99.00 %, 849.70, 77.62, 0.09, and 99.38 %, respectively; and for CMR, 80.00 %, 99.00 %, 187.54, 24.21, 0.17, and 97.71 %, respectively. The authors concluded that in patients with atrial fibrillation (AF), CMR has been proven to be a favorable diagnostic technique for the detection and assessment of LA/LAA thrombus. Among the imaging sequences evaluated, DE-CMR had the highest sensitivity, specificity, and diagnostic accuracy.

Management of Cardiovascular Complications of Cancer Therapy:

Tamene and colleagues (2015) stated that patients with cancer are subject to short-term and long-term adverse cardiovascular outcomes from cancer therapies. It is important to identify patients at risk for cardiotoxicity so that appropriate therapy can
be instituted early. Cardiovascular MRI is emerging as a promising imaging modality with unique applications beyond standard left-ventricular (LV) systolic function assessment.

In a prospective study, de Ville de Goyet and associates (2015) examined the role of cardiac MRI in the detection of subclinical left or right ventricular dysfunction as well as the prevalence of myocardial scaring in patients undergoing cancer treatments. A total of 81 children were enrolled in a pre-chemotherapy and then in a yearly protocol including: clinical evaluation; laboratory evaluation; electrocardiogram; echocardiogram; and cardiac MRI. Early LV systolic dysfunction was only detected in 2 patients. The entire cohort presented a significant increase of the left atrial volume as measured by cardiac MRI. This finding correlated with the total cumulative dose of anthracyclines ($r = 0.34; p < 0.05$) and the mean LV radiation dose ($r = 0.86; p < 0.05$). These investigators also observed a mild increase of myocardial scaring, similarly correlated to the radiation dose ($r = 0.85; p < 0.05$).

The authors concluded that screening tools for late-onset cardiomyopathy secondary to cancer treatment are lacking. They stated that the findings of this study support the use of cardiac MRI for the evaluation of the left atrial volume, as an early marker of diastolic dysfunction, and myocardial delayed enhancement, as a marker of myocardial fibrosis and scaring. Moreover, they stated that longer follow-up and larger studies are still needed to better define the role of cardiac MRI in the evaluation of childhood cancer survivors.

In a review on “Cardiotoxicity of anticancer treatments: Epidemiology, detection, and management” (Curigliano et al, 2016), cardiac MRI was not mentioned as a detection/management tool.

The Canadian Cardiovascular Society’s guidelines for “Evaluation and management of cardiovascular complications of cancer therapy” (Virani et al, 2016) did not mention cardiac MRI as a management tool.

Jeong and co-workers (2017) stated that cardiac MRI is emerging as an important diagnostic modality in the management of cardiovascular-related dysfunction in oncological diseases. Advances in imaging techniques have enhanced the detection and evaluation of cardiac masses; meanwhile, innovative applications have created a growing role for cardiac MRI for the management of cardiotoxicity caused by cancer therapies. These investigators provided an overview of the clinical indications and technical considerations of cardiac MRI. Its role in the
evaluation of cardiac masses and cardiac function was reviewed, and novel sequences were discussed that are giving rise to future directions in cardio-oncology research. A review of the literature was also performed, focusing on cardiac MRI findings associated with cardiac dysfunction related to cancer treatment. Cardiac MRI can be used to differentiate benign and malignant primary cardiac tumors, metastatic disease, and pseudo-tumors with high spatial and temporal resolution.

Cardiac MRI can also be used to detect the early and long-term effects of cardiotoxicity related to cancer therapy. This was accomplished through a multi-parametric approach that used conventional bright blood, dark blood, and post-contrast sequences while also considering the applicability of newer T1 and T2 mapping sequences and other emerging techniques. The authors concluded that cardio-oncology programs have an expanding presence in the multi-disciplinary approach of cancer care. Consequently, knowledge of cardiac MRI and its potential applications is critical to the success of contemporary cancer diagnostics and cancer management.

Gavila and colleagues (2017) evaluated the difference between what is currently done and what standards of care should be used to minimizing and managing cardiac toxicity in breast cancer survivors. A 2-round multi-center Delphi study was carried out. The panel consisted of 100 oncologists who were asked to define the elected therapies for breast cancer patients, the clinical definition and patterns of cancer drug-derived cardiac toxicity, and those protocols focused on early detection and monitoring of cardiovascular outcomes. Experts agreed a more recent definition of cardiotoxicity. Around 38 % of patients with early-stage disease, and 51.3 % cases with advanced metastatic breast cancer had pre-existing risk factors for cardiotoxicity. Among risk factors, cumulative dose of anthracycline greater than or equal to 450 mg/m2 and its combination with other anti-cancer drugs, and a pre-existing cardiovascular disease were considered the best predictors of cardiotoxicity. Echocardiography and radionuclide ventriculography have been the proposed methods for monitoring changes in cardiac structure and function. Breast cancer is generally treated with anthracyclines (80 %), so that the panel strongly stated about the need to plan a strategy to managing cardiotoxicity. A decline of LV ejection fraction (LVEF) of greater than 10 %, to an LVEF value less than 53 % was suggested as a criterion for changing the dose schedule of anthracyclines, or suspending the treatment of chemotherapy plus trastuzumab until the normalization of the LV function. The use of liposomal anthracyclines was strongly suggested as a therapeutic option for breast cancer patients. The authors concluded that this report was the first to produce a set of statements on the prevention, evaluation and
monitoring of chemotherapy-induced cardiac toxicity in breast cancer patients.

Furthermore, an UpToDate review on "Clinical utility of cardiovascular magnetic resonance imaging" (Fuisz and Pohost) does not mention cardiac MRI as a management tool.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>75557</strong></td>
<td>Cardiac magnetic resonance imaging for morphology and function without contrast material</td>
</tr>
<tr>
<td><strong>75559</strong></td>
<td>with stress imaging</td>
</tr>
<tr>
<td><strong>75561</strong></td>
<td>Cardiac magnetic resonance imaging for morphology and function without contrast material(s), followed by contrast material(s) and further sequences</td>
</tr>
<tr>
<td><strong>75563</strong></td>
<td>with stress imaging</td>
</tr>
<tr>
<td><strong>75565</strong></td>
<td>Cardiac magnetic resonance imaging for velocity flow mapping</td>
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Other CPT codes related to the CPB:

<table>
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<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>71250 - 71270</td>
<td>Computed tomography, thorax</td>
</tr>
<tr>
<td>71550 - 71552</td>
<td>Magnetic resonance (e.g., proton) imaging, chest (e.g., for evaluation of hilar and mediastinal lymphadenopathy)</td>
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<tr>
<td>76604</td>
<td>Ultrasound, chest (includes mediastinum), real time with image documentation</td>
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<tr>
<td>77058 - 77059</td>
<td>Magnetic resonance imaging, breast, without and/or with contrast material(s)</td>
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<tr>
<td>78414 - 78499</td>
<td>Nuclear medicine, cardiovascular system imaging</td>
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HCPCS codes covered if selection criteria are met:

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<td>A9576</td>
<td>Injection, gadoteridol, (ProHance multipack), per ml</td>
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<td>A9577</td>
<td>Injection, gadobenate dimeglumine (MultiHance), per ml</td>
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<tr>
<td>A9578</td>
<td>Injection, gadobenate dimeglumine (MultiHance multipack), per ml</td>
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<tr>
<td>A9579</td>
<td>Injection, gadolinium based magnetic resonance contrast agent, not otherwise specified, per ml</td>
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<tr>
<td>Code</td>
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<td>Other HCPCS codes related to the CPB:</td>
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<tr>
<td>J0151</td>
<td>Injection, adenosine for diagnostic use, 1 mg (not to be used to report any adenosine phosphate compounds, instead use A9270)</td>
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<td>ICD-10 codes covered if selection criteria are met (not all-inclusive):</td>
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<td>A18.89</td>
<td>Tuberculosis of other sites [myocardium]</td>
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<td>A36.81</td>
<td>Diphtheritic cardiomyopathy</td>
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<td>A39.52</td>
<td>Meningococcal myocarditis</td>
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<td>Cardiovascular and cerebrovascular syphilis</td>
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<td>Viral myocarditis</td>
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<td>B58.81</td>
<td>Toxoplasma myocarditis</td>
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<td>Malignant neoplasm of bronchus and lung, thymus, heart, mediastium and pleura</td>
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<td>C45.0</td>
<td>Mesothelioma of pleura and pericardium</td>
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<td>C45.2</td>
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<td>Secondary malignant neoplasm of lung, mediastinum and pleura</td>
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<td>Benign neoplasm of thymus, heart and mediastinum</td>
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<td>D15.2</td>
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<td>D17.4</td>
<td>Benign lipomatous neoplasm of intrathoracic organs</td>
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<td>D19.0</td>
<td>Benign neoplasm of mesothelial tissue of pleura</td>
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<td>D21.3</td>
<td>Benign neoplasm of connective and other soft tissue of thorax</td>
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<td>Neoplasm of uncertain behavior of trachea, bronchus, lung, pleura, mediastinum and thymus</td>
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<td>Other diseases of pulmonary vessels</td>
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<td>J94.0 - J94.9</td>
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<tr>
<td>K75.1</td>
<td>Phlebitis of portal vein</td>
</tr>
<tr>
<td>Q20.0 - Q28.9</td>
<td>Congenital malformations of the circulatory system</td>
</tr>
<tr>
<td>Q87.40 - Q87.43</td>
<td>Marfan's syndrome</td>
</tr>
<tr>
<td>R09.1</td>
<td>Pleurisy</td>
</tr>
<tr>
<td>R22.2</td>
<td>Localized swelling, mass and lump, trunk</td>
</tr>
<tr>
<td>R93.1</td>
<td>Abnormal findings on diagnostic imaging of heart and coronary circulation</td>
</tr>
<tr>
<td>R93.8</td>
<td>and other specified body structures</td>
</tr>
<tr>
<td>R94.31</td>
<td>Abnormal electrocardiogram [ECG] [EKG]</td>
</tr>
<tr>
<td>T82.817+ - T82.818+</td>
<td>Embolism of cardiac and vascular prosthetic devices, implants and grafts</td>
</tr>
<tr>
<td>Z98.61</td>
<td>Coronary angioplasty status</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I74.3</td>
<td>Embolism and thrombosis of arteries of the lower extremities</td>
</tr>
<tr>
<td>I75.021 - I75.029</td>
<td>Atheroembolism of lower extremity</td>
</tr>
<tr>
<td>T86.20 - T86.23</td>
<td>Complications of heart transplant</td>
</tr>
<tr>
<td>Z13.6</td>
<td>Encounter for screening for cardiovascular disorders [routine without signs or symptoms of disease]</td>
</tr>
<tr>
<td>Z94.1</td>
<td>Heart transplant status</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

http://qawww.aetna.com/cpb/medical/data/500_599/0520_draft.html 08/19/2018


22. Kramer CM. Magnetic resonance imaging to identify the high-risk plaque. Am J Cardiol. 2002;90(10C):15L-17L.


25. Ontario Ministry of Health and Long-Term Care, Medical Advisory Secretariat. Functional cardiac magnetic resonance imaging in the assessment of myocardial viability and perfusion. Health Technology


32. Beanlands RS, Chow BJ, Dick A, et al; Canadian Cardiovascular Society; Canadian Association of Radiologists; Canadian Association of Nuclear Medicine; Canadian Nuclear Cardiology Society; Canadian Society of Cardiac Magnetic Resonance. CCS/CAR/CANM/CNCS/CanSCMR joint position statement on advanced noninvasive cardiac imaging using positron emission tomography, magnetic resonance imaging and


44. Chen S, Cunningham J. Magnetic resonance imaging for patients with valvular heart disease: A review of clinical-effectiveness. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); 2009.
45. Murphy G, Argaez C. Cardiac Magnetic Resonance Imaging (MRI) for patients with coronary artery disease: A review of diagnostic accuracy. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); 2009.


53. Ammash NM, Connolly HM. Ventricular septal defect in adults. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed April 2013.


56. Mckenna MJ. Cardiac sarcoidosis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed April 2013.

57. Scott PA, Rosengarten JA, Curzen NP, Morgan JM. Late gadolinium enhancement cardiac magnetic resonance imaging for the prediction of


63. Fuisz AR, Pohost GM. Clinical utility of cardiovascular magnetic resonance imaging. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed March 2015.


86. Fuisz AR, Pohost GM. Clinical utility of cardiovascular magnetic resonance imaging. UpToDate Inc., Waltham, MA. Last reviewed March 2018.

Amendment to
Aetna Clinical Policy Bulletin Number:
0520 Magnetic Resonance Imaging of the Cardiovascular System - Cardiac MRI

There are no amendments for Medicaid.