UTILITY OF DELAYED ENHANCED CARDIAC MAGNETIC RESONANCE IN THE ASSESSMENT OF CARDIOMYOPATHIES

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INTRODUCTION

Heart failure is a major public health problem in the United States, with more than five million individuals afflicted and well over 600,000 new cases diagnosed each year.1 The estimated direct and indirect cost of heart failure is nearly $35 billion for 2008 alone. While coronary artery disease (CAD) is the leading cause of left ventricular (LV) dysfunction, anywhere from a third to one-half of all patients have LV dysfunction in the absence of significant epicardial CAD.2 Most of these patients are labeled with the general diagnosis of idiopathic nonischemic cardiomyopathy (NICMP), as no direct discernible etiology of their myocardial dysfunction is evident. Identifying the specific etiology of HF in these patients can have important prognostic implications.3 However, traditional imaging modalities such as echocardiography, nuclear scintigraphy, or coronary angiography are limited in their ability to specifically evaluate the myocardium and characterize tissue. In fact, even the utility of endomyocardial biopsy is uncertain because of frequent nonspecific findings and the inherent invasiveness and small but finite risk of the procedure.[4]

In recent years, delayed contrast enhancement cardiac magnetic resonance (DE-CMR) has emerged as a powerful noninvasive technique for directly assessing myocardial structure and tissue characterization. Studies have demonstrated its ability to detect both irreversible acute ischemic injury and chronic myocardial infarction with a high level of accuracy.s-11 Using this same technique in patients with NICMP, we have been able to detect unique patterns of myocardial scarring that aid in identifying a specific etiology of NICMP, thereby providing additional prognostic information and occasionally drastically altering patient management. This article will describe the potential role of DE-CMR in assessing patients with cardiomyopathy.

ISCHEMIC VS. NONISCHEMIC CARDIOMYOPATHY

The initial study describing del$_{ay}$ed enhancement findings in nonischemic cardiomyoparhy was published by Wu et al.[8] In this study, none of the 20 patients with idiopathic dilated cardiomyopathy were found to have hyperenhancemem. One important stipulation to keep in mind is chat although there was significant LV dysfunction in chis cohort, the duration of heart failure was rather short as many were enrolled at the first onset of heart failure. A more recent srudy by McCrohon et al12 examined a larger population of 90 patients with chronic heart failure and LV dysfunction - 63 with idiopathic dilated cardiomyopathy and 27 with ischemic cardiomyopathy. All patients had coronary angiography as part of their diagnostic workup. Of the 27 patients with ischemic cardiomyoparhy, all had a history of myocardial infarction. Thus, it is perhaps not surprising that all 27 had myocardial hyperenhancement. The pattern of hyperenhancement involved the subendocardium in all patients. Of the 63 patients with idiopathic dilated cardiomyopathy, 59% had no hyperenhancement, 13% had hyperenhancement involving the subendocardium (similar to that found in ischemic cardiomyoparhy), and 28% had hyperenhancement in an unusual pattern, primarily involving the ventricular midwall with subendocardial sparing.

In a recent study we evaluated 45 patients with symptomatic heart failure and evidence of significant LV systolic dysfunction (LVEF <35% on invasive ventriculography or echocardiography); 28 patients had ischemic cardiomyopathy and 17 had idiopathic dilated cardiomyopathy. In chis study, hyperenhancement patterns consistent with prior myocardial infarction were identified; linear midwall striae with increased image imensitywere not scored as hyperenhanced regions. Interestingly, the findings demonstrated that all patients wirh ischemic cardiomyopathy had hyperenhancement, whereas only 12% of patients with idiopathic dilated cardiomyopachy had hyperenhancemenr. When we tested clinical parameters for their utility in distinguishing ischemic from nonischemic cardiomyopathy, we found char the presence of Q-waves on 12-lead electrocardiography was moderately specific {82%) but insensitive (46%) for the identification of ischemic disease (overall accuracy, 60%). The presence of regional (as opposed to global) dysfunction on cine MRI was also a poor discriminator of the etiology of heart failure (overall accuracy, 47%). The best discriminator was the presence of hyperenhancemenr on DE-CMR, which had a 100% sensitivity, 88% specifici$_{ry}$, and 96% overall accuracy for the detection of ischemic disease.

In this study, 100% of patients with ischemic cardiomyopathy had evidence

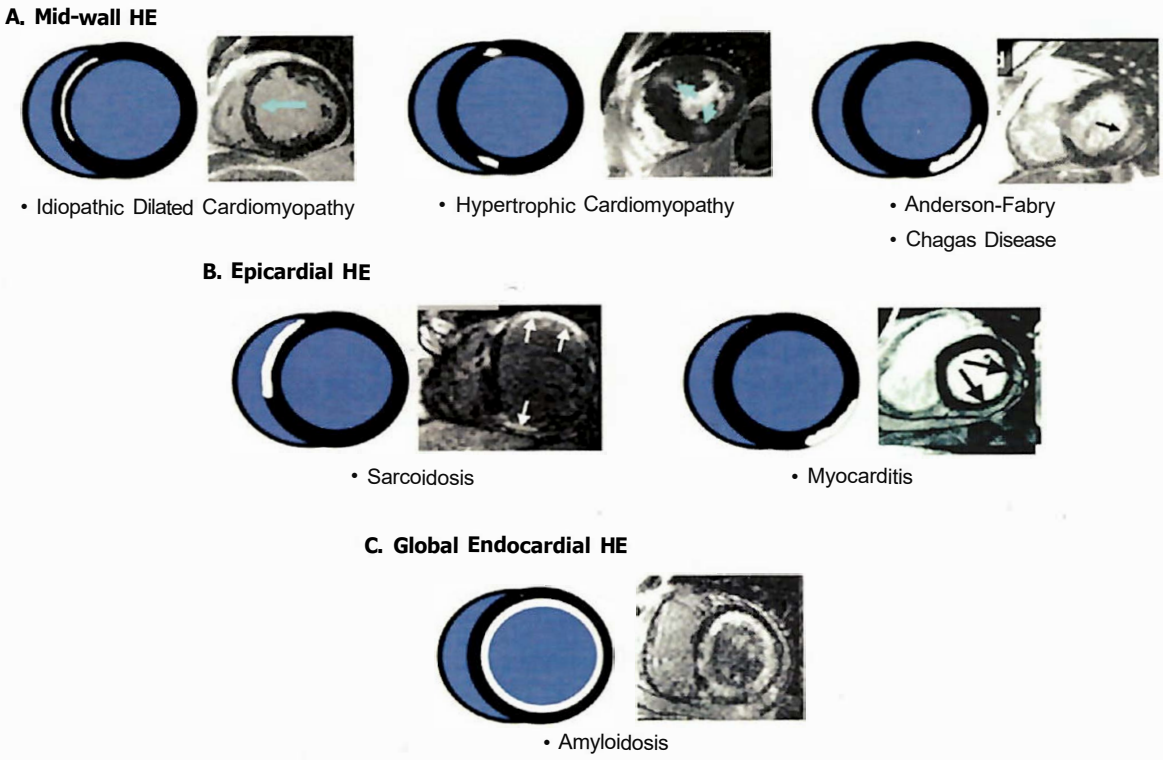

Figure 1. Characteristic patterns of hyperenhancement (scarring) in various forms of nonischemic cardiomyopathy; see text for details. Adapted from Shah OJ, Judd RM, Kim RJ. In: Edelman RR, Hesselink JR (eds). *Clinical Magnetic Resonance Imaging;* 3rd ed. New York: Elsevier Press; 2005.

of hyperenhancement despite the fact that only 50% had a clinical history of myocardial infarction. This finding is consistent with necropsy studies demonstrating chat virtually all patients with congestive heart failure and significant coronary artery disease have gross myocardial scarring at auwpsy, even those without a clinical history of MI, angina, or Q-waves.[13-14] Conversely, we observed in patients with idiopathic dilated cardiomyoparhy chat hyperenhancement was uncommon. This finding is also consistent with previous studies. Roberts et al15 found grossly visible scars at cardiac necropsy in 14% of patients with idiopathic dilated cardiomyopathy. Uretsky et al.[16] evaluated chronic heart failure patients at autopsy and found old infarcts in 12% of patients without coronary artery disease (CAD). A number of mechanisms may be responsible for myocardial infarction in patients without CAD, including coronary vasospasm, thrombosis with spontaneous lysis superimposed on minimal atherosclerosis, or coronary emboli. Regardless of the mechanism, myocardial infarction in the absence of CAD is rare, and the findings in this study suggest that DE-CMR may be useful in distinguishing ischemic from nonischemic cardiomyopathy noninvasively. One caveat, however, should be noted. The non-CAD cohort **in** the studies by Wu, McCrohon, and Bello included only patients **with** idiopathic dilated cardiomyoparhy, as patients with other forms of nonischemic cardiomyopathy such as hypertrophic cardiomyopachy, myocarditis, and infiltrative cardiomyopathy were excluded at the rime of enrollment.

HYPERTROPHIC CAR DIOMYOPATHY

Hypemophic cardiomyopachy (HCM) is the most frequently occurring generic cardiomyopathy.[17] According co current data, echocardiography missed the diagnosis in 6% of suspected HCM patients.[18] Recently, several studies have described DE-CMR findings in patients with HCM. Choudhury et al19 enrolled 21 patients who were thought co be representative of the majority of community patients with HCM, since they were identified by routine outpatient screening procedures and were generally asymptomatic or minimally symptomatic. Patients with concomitant CAD were excluded. In this study, cine MRI demonstrated that the maximum LV end-diastolic wall thickness averaged 25±8mm, and rhe LV ejection fraction was preserved (70± 11%).

DE-CMR demonstrated chat hyperenhancement was found in the majority of patients (81%), and hyperenhancement mass was on average 8±9% of the left ventricular mass. The pattern of hyperenhancement, however, was peculiar. Hyperenhancement occurred only in hypertrophied regions, was patchy with multiple foci, and predominately involved the middle third of the ventricular wall. Additionally, all patients with hyperenhancement had involvement at the junctions of the imervemricular septum and the RV free wall (Figure 1). On a regional basis, there was a modest correlation between the extent of hyperenhancemenc and end-diastolic wall thickness (r=0.36, p<0.0001). No region with end-diastolic wall thickness <10 mm had any hyperenhancement. There was also a significant but inverse correlation between the extent of hyperenhancement and systolic wall thickening (r=-0.21, p<0.0001).

Although a number of pathophysiological processes are evident in hypercrophic cardiomyopathy, Choud hury et al. interpreted hyperenhancemenc in HCM as specifically representing myocardial scarring. The rationale for this assumption is discussed at length in a recent editorial.[20] New data by Moon et al.[21] suggests that this assumption is valid. In a patient that underwent heart transplantation after in vivo DE-CMR, followed by detailed histological anal$_{y s}$is of the explanted heart, there was a significant regional relationship between the extent of hyperenhancement and the amount of myocardial fibrosis (r=0.7, p<0.0001) but not disarray. While the occurrence of scarring in HCM has been previously described by multiple studies, these reports all involved highly selected patient cohorts, such as those suffering sudden death (necropsy studies) or those undergoing surgical myomectomy for refractory symptoms.[22-28] The study by Choudhury et al. was the first to demonstrate that myocardial scarring was common in a living cohort who was likely representative of the majority of HCM patients.

In a more recent study, Moon et al.[29] performed DE-CMR in 53 patients selected from a dedicated HCM clinic. Overall, hyperenhancement was found in 79% of patients, a figure quire similar to that found by Choudhu$_{r y}$ et al. This study, however, also compared DE-CMR findings to the presence of clinical risk factors for sudden death in HCM (e.g., nonsustained ventricular tachycardia, syncope, family history of premature cardiac death, etc.), and to progressive adverse LV remodeling. Interestingly, the authors observed that there was a greater extent of hyperenhancement in patients with two or more risk factors for sudden death (15.7% vs. 8.6%, p=0.02) and in patients with progressive remodeling (28.5% vs. 8.7% of LV mass, p<0.001).

Since hyperenhancement was observed in approximately 80% of patients in both of the above studies, the presence of hyperenhancement in itself cannot be indicative of an adverse prognosis. However, it is possible that the amount ofhyperenhancement - indicative of the amount of scarring - may be an important prognostic determinant. Further studies are underway at our institution to test this hypothesis.

MYOCARDITIS

Clinical manifestation of myocarditis or inflammatory cardiomyopathy varies, with a broad spectrum of symptoms ranging from asymptomatic to signs of myocardial infarction and cardiogenic shock. Myocarditis can occasionally lead to sudden death and may progress to dilated cardiomyopathy in up to 10% of patients.[30] Endomyocardial biopsy is considered a gold standard for diagnosis. However, it is an invasive procedure and has limited sensitivity and specificity. A noninvasive and effective diagnostic imaging modali$_{t y}$ is CMR. Cine imaging shows wall motion abnormalities that are matched by areas of scar on DE-CMR. The scar pattern frequently involves the epicardial myocardium of the lateral wall.

Mahrholdt et al.[30] performed DE-CMR in 32 patients who were diagnosed with myocardiris. Hyperenhancemem was found in 28 of 32 patients (88%). Of the 21 patients in whom myocardial biopsy was obtained from the region of hyperenhancemem, histoparhological analysis revealed active myocardiris in 19. Of the remaining 11 patients in whom biopsy could not be taken from the region of hyperenhancement (hyperenhancement could not be reached by bioptome in seven; no hyperenhancemenc was present in four), active myocarditis was found in only one. Hyperenhancement was usually observed in a patchy distribution originating primarily from the epicardial quartile of the wall with one or several foci (Figure 1). Additionally, there was a predilection for the lateral free wall. The pattern and distribution of hyperenhancemem found in this study are consistent wich the pattern and distribution of myocardial lesions found in postmortem evaluations of patients with myocarditis.31 The potential mechanism for hyperenhancement in myocardiris was postulated to be similar to that for coronary artery disease: either acute necrosis with cell membrane rupture for acute lesions, or myocardial scarring and fibrosis for chronic lesions. If true, chis mechanism would imply char the presence, location, and total extent of irreversible myocardial damage that occurs in a patient with myocarditis could be determined noninvasively by DE-CMR.

ANDERSON-FABRY DISEASE

Anderson-Fab$_{r y}$ disease, an X-linked lysosomal storage disorder of glycosphingolipidmetabolism,isacauseofidiopathic LV hypertrophy. Although the severity of cardiac involvement is variable, affected patients can have cardiomyopathy, valvular disease, dysrhythmias, and CAD. Moon et al.[32] studied 18 men and eight women heterozygotes with this condition. Hyperenhancement

was found in 50% of men and 50% of women, although the extent of hyperenhancement was greater in men (7.7% versus 4.6% of LV mass). In 12 of those 13 patients, the location of hyperenhancement was the basal inferolateral wall; in eight, the involvement was distinctly in a non-CAD pattern since the subendocardium was spared (Figure 1). A follow-up study demonstrated hiscologic correlation between hyperenhancement and extracellular collagen deposition.33

CARDIAC AMYLOIDOSIS

Cardiac involvement is seen with primary amyloidosis (AL) and is an example of infiltrative cardiomyopathy.34 Cardiac AL is associated with a median survival of six months.34-35 Diagnosis of cardiac involvement requires multiple endomyocardial biopsies, wirh each biopsy specimen having a 55% sensitivity for the detection of amyloid protein deposition.36 As a noninvasive diagnostic cool, CMR can aid in identifying patients with cardiac AL (Figure 1). According to Maceira et al., there was 97% concordance in che diagnosis of cardiac AL by combining the presence of late gadolinium enhancement and an optimized Tl threshold.[37] More recently, Vogelsberg et al.[38] studied a series of patients with heart failure and restrictive filling pattern; all patients underwent DE-CMR and endomyocardial biopsy. They found chat DE-CMR demonstrated an 80% sensitivity and 92% specificity for the detection of cardiac amyloid involvement.

SARCOIDOSIS

Myocardial involvement is evident in about 5% of patients with sarcoidosis; however, autopsy studies have shown up to 50% of cases of noncaseating granulomas in fatal sarcoidosis.[39] In one study by Smedema et al., CMR was used to evaluate cardiac sarcoidosis in 58 patients with biopsy proven pulmonary sarcoidosis, and it showed hyperenhancement primarily involving the basal and lateral segments in 19 patients.[40] The sens1t1v1ty and specificity of CMR were 100% and 78% respectively. We hypothesize chat the presence and extent of hyperenhancement on DE-CMR may be directly related to the risk of sudden cardiac death, a leading cause of mortality in chis population.[41]

RISK STRATIFICATION FOR SUDDEN DEATH

Scarred myocardium is an established anatomical and electrophysiological substrate for the occurrence of ventricular tachyarrhythmias and sudden death in patients with CAD.42 The ability of DE-CMR to accurately detect the presence and extent of scarred myocardium may make it uniquely suited to noninvasively identify individuals with substrate for sudden death. Some recent pilot data comparing DE-CMR findings co results of electrophysiological studies (EPS) suggests that this hypothesis is valid.43 For example, of the 58 patients studied, 18 were determined by EPS to be at high risk for sudden death (inducible monomorphic ventricular tachycardia (VT]), and all 18 showed myocardial scarring on DE-CMR. Conversely, none of the 22 patients without scarring had inducible monomorphic VT. On multivariate analysis, scar size by DE-CMR was found to be the best independent predictor of inducibility at EPS.

Earlier in chis section, we noted that hyperenhancement can be observed in patients with nonischemic cardiomyopathy, particularly in those with hypertrophic and infiltrative forms of disease. Although there is currently less evidence linking scarred myocardium to sudden death in patients without CAD, there is reason to believe that scar tissue can serve as substrate for malignant ventricular tachyarrhythmias in these patients as well.[20] Therefore, we hypothesize that DE-CMR will provide important prognostic information for patients with a wide range of myocardial disorders. Studies are currently underway at our institution to evaluate a potential relationship between sudden cardiac death and the presence, extent, or morphology of myocardial scar.

CONCLUSION

Delayed enhancement CMR is proving to be an invaluable cool in the evaluation of patients with cardiomyopathy. A number of studies have demonstrated its ability co identify unique patterns of enhancement in varying forms of nonischemic cardiomyopathy. A significant amount of work is currently underway at our institution and others to fully define CMR's potential to aid in the evaluation and management of patients with cardiomyopathy.

REFERENCES

1. *Rosamond W, Flegal K, Furie K, et al. Heart Disease and Stroke Statistics 2008 Update. A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2007;117(4):e25-146.*
2. *Fox KF, Cowie MR, Wood DA, et al. Coronary artery disease as the cause of incident heart failure in the population. Eur Heart] 2001;22(3):228-236.*
3. *Felker GM, Thompson RE, Hare JM, et al. Underlying causes and long-term survival in patients with initially unexplained cardiomyopathy. N Engl J Med. 2000;342(15):1077-1084.*
4. *Hunt SA, Abraham WT, Chin MH, et al. ACCIAHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): devewped in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Tramplantation: endorsed by the Heart Rhythm Society. Circulation. 2005;112(12}:el54-235.*
5. *Kim Rf, Fieno DS, Parrish TB, et al. Re/atiomhip of MRI delayed contrast*

enhancement to irreversible injury, infarct age, and contractile Junction. Circulation. 1999;100(19}:1992-2002.

6. Fieno DS Kim Rf. Chen EL, LomasneyJW, Klocke Ff. Judd RM. Contrast-enhanced magnetic resonance imaging of myocardium at risk: distinction between reversible and irreversible injury throughotlt infarct healing. J Am Coll Cardiol. 2000;36(6):1985-1991.

7. Ricciardi MJ. Wu E, Davidson CJ, et al. Visualization of discrete microinfarction after percutaneous coronary intervention associated with mild creatine kinase-MB elevation. Cirrnlation. 2001;103(23):2780-2783.

8. Wu E, Judd RM, Vargas JD, Klocke Ff. Bonow RO, Kim Rf. Visualisation of presence, location, and transmural extent of healed Q-wave and non-Q-wave myocardial infarction. Lancet. 2001;357(9249):21-28.

9. Choi KM, Kim Rf. Gubernikojf G, VafKas JD, Parker M, Judd RM. Trammural extent of acute myocardial infarction predicts long-term improvement in contractile Junction. Circulation. 2001;104(10):1101-1107.

JO. Hillenbrand HB, Kim Rf. Parker MA, Fieno DS, Judd RM. Early assessment of myocardial salvage by contrast-enhanced magnetic resonance imaging. Cirrnlation. 2000;102(14):1678-1683.

11. Kim Rf, Wu E. Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med. 2000;343(20):1445-1453.

12. McCrohon JA, Moon JC, Prasad SK. et al. Differentiation of heart failure related to dilated cardiomyopathy and coronary artery disease using gadolinium-enhanced cardiovascular magnetic resonance. Circulation. 2003;108(1):54-59.

13. Schuster EH, Bulkley BH. Ischemic cardiomyopathy: a c/inicopathologic study offourteen patients. Am Heart J 1980;100(4):506-512.

14. Boucher CA, Fallon JT, Johnson RA, Yurchak PM. Cardiomyopathic syndrome caused by coronary artery disease. III: Prospective clinicopathological study of its prevalence among patients with c/inicaly unexplained chronic heart failure. Br HeartJ. 1979;41(5):613-620.

15. Roberts WC, Siegel Rf, McManus BM. Idiopathic dilated cardiomyoparhy: analysis of 152 necropsy patients. Am J Cardiol. 1987;60(16):1340-1355.

/6. Uretsky BF. Thygesen K, Armstrong PW, et al. Acute coronary findings at autopsy in heart failure patients with sudden death: results from the asJessment of treatment with lisinopril and survival (ATLAS) trial. Circulation. 2000;102(6):611-616.

17. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. JAMA. 2002;287(10):1308-1320.

18. Rickers C, Wilke NM, jerosch-Herold M, et al. Utility of cardiac magnetic resonance imaging in the diagnosis of hypertrophic cardiomyopathy. Circulation. 2005;112(6):855-861.

19. Choudhury L, Mahrholdt H, Wagner A, et al. Myocardial scarring in asymptomatic or mildly symptomatic patients with hypertrophic cardiomyopathy. J Am Coll Cardio/. 2002;40(12):2156-2164.

20. Kim Rf, Judd RM. Gadolinium-enhanced magnetic resonance imaging in hypertrophic cardiomyopathy: in vivo imaging of the pathologic substrate for premature cardiac death? J Am Coll Cardiol. 2003;41(9):1568-1572.

21. Moon JC. Reed E, Sheppard MN, et al. The histologic basis of late gadolinium enhancement cardiovascular magnetic resonance in hypertrophic cardiomyopathy. J Am Coll Cardiol. 2004;43(12):2260-2264.

22. Maron BJ, Epstein SE, Roberts WC. Hypertrophic cardiomyopathy and transmural myocardial infarction without significant atherosclerosis of the extramural coronary arteries. A m] Cardio/. 1979;43(6):1086-1102.

23. Maron BJ, Wolfion JK. Epstein SE, Roberts WC. Intramural ("small vessel") coronary artery disease in hypertrophic cardiomyopathy. J Am Coll Cardiol. 1986; 8(3):545-557

24. Basso C, Thiene G, Corrado D, Buja G, Melacini P, Nava A. Hypertrophic cardiomyopathy and rndden death in the young: pathologic evidence of myocardial ischemia. Hum Pathol. 2000;31(8):988-998.

25. Unver.ferth DV, Baker PB, Pearce LI, Lautman J, Roberts WC. Regional myocyte hypertrophy and increased interstitial myocardial fibrosis in hypertrophic cardiomyopathy. Am J Cardiol. 1987;59(9):932-936.

26. Roberts CS, RobertJ WC. Hypertrophic cardiomyopatky as a cause of massive cardiomegaly (greater than 1,000 g). Am J Cardiol. 1989;64(18):1209-1210.

27. Kuribayashi T, Roberts WC. Myocardial disarray at junction of ventricular septum and left and right ventricular free walls in hypertrophic cardiomyopathy. Am J Cardiol. 1992;70(15):1333-1340.

28. Davies MJ, McKenna WJ Hypertrophic cardiomyopathy--patholo$_{gy}$ andpathogenesis. Histopatholo$_{gy}$. 1995;26(6):493-500.

29. Moon JC. McKenna Wj, McCrohor, JA, Elliott PM, Smith GC, Pennell DJ. Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. J Am Coll Cardiol. 2003;41(9):1561-1567

30. Mahrholdt H, Goedecke C, Wagner A, et al. Cardiovasrnlar magnetic resonance assessment of human myocarditis: a comparison to histolo$_{gy}$ and molecular pathology. Circulation. 2004;109(10):1250-1258.

31. Shirani j, Freant Lj, Roberts WC. Gross and semiquantitative histologic findi$_{ngs}$ in mononuclear cell myocarditis causing sudden death, and implications for er,domyocardial biopsy. Am J Cardiol. 1993;72(12):952-957

32. Moon JC, Sachdev B, Elkington AG, et al. Gadolinium enhanced cardiovascular magnetic resonance in Anderson-Fab$_{ry}$ disease. Evidence for a disease specific abnormality of the myocardial interstitium. Eur HeartJ 2003;24(23):2151-2155.

33. Moon JC. Sheppard M, Reed E, Lee P, Elliott PM, Pennell DJ The histological basis of late gadolinium enhancement cardiovascular magnetic resonance in a patient with Anderson-Fab$_{ry}$ disease. J Cardiovasc Magn Reson. 2006;8(3):479-482.

34. Falk RH, Comenzo RL, Skinner M. The systemic amyloidoses. N Englj Med. 1997;337(13):898-909.

35. Falk RH. Diagnosis and management of the cardiac amyloidoses. Circulatior,.

2005;112(13):2047-2060.

36. *Pellikka PA, Holmes DR Jr, Edwards WD, Nishimura RA, Tajik A], lvjle RA. Endomyocardial biopsy in 30 patients with primary amyloidosis and suspected cardiac involvement. Arch Intern Med. 1988;148(3):662-666.*
37. *Maceira AM, Joshi], Prasad SK, et al. Cardiovascular magnetic resonance in cardiac amyloidosis. Circulation. 2005; 111(2):186-193.*
38. *Vogelsberg H, Mahrholdt H, Deluigi CC, et al. Cardiovascular magnetic resonance in clinically suspemd cardiac amyloidosis: noninvasive imaging compared to endomyocardial biopsy. J Am Coll Cardiol. 2008;51(10):1022-1030.*
39. *Sharma OP, Maheshwari A, Thaker K Myocardial sarcoidosis. Chest. 1993; 103(1):253-258.*
40. *Smedema JP, Snoep G, van Kroonenburgh MP, et al. The additional value of gadolinium-enhanced MRI to standard assessmentfor cardiac involvement in patients with pulmonary sarcoidosis. Chest. 2005;128(3):1629-1637.*
41. *Virmani R, Bures JC, Roberts WC. Cardiac sarcoidosis: a major cause of sudden death in young individuals. Chest. 1980;77(3):423-428.*
42. *Hurwitz JL, Josephson ME. Sudden cardiac death in patients with chronic coronary heart disease. Circulation. 1992;85(1 Suppl}:143-49.*
43. *Klem l Weimaft J, Heitner JP, et al. The utility of contrast-enhanced MRI for screening patients at risk for malignant ventricular tachyarrhythmias. J Cardiovasc Magn Reson. 2004;6(1}:84*