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Research Paper

Evaluation of cardiac structures and function in hypertrophic cardiomyopathy with magnetic resonance imaging

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Abstract

Objective: To assess the capability of magnetic resonance imaging(MRI) in evaluating the cardiac structures and function in the hypertrophic cardiomyopathy(HCM). **Methods:**Fourteen healthy volunteers and eighteen cases with HCM verified by history, clinical presentation, electrocardiogram and echocardiography(ECG) were performed with MRI. The myocardial thickness of interventricular septum at the basal segment and that of posterolateral free wall of the left ventricle(LV) were measured. Some indexes for evaluating cardiac function were measured using ARGUS auto-quantitative program. **Results:**The myocardial thickness of septum at the basal segment had significant difference between the HCM patients and the healthy volunteers. There was no significant difference between MRI and ECG in examining end-diastolic volume, ejection fraction of the LV. **Conclusion:**MRI can fully provide more information on the abnormalities of cardiac anatomy and function; thus, it is of great value in clinical application.

Key words: hypertrophic cardiomyopathy; magnetic resonance imaging; ECG

INTRODUCTION

Hypertrophic cardiomyopathy is a kind of disease with unknown reason and asymmetric hypertrophy of myocardium. In the past, the diagnoses depend mainly on history, symptom, echocardiography(ECG) exam and excluding the other cardiac diseases. Now, with the great progress of magnetic resonance imaging(MRI), especially the ultra-fast software [1], the evaluation of cardiac structures and function scanned by MRI is applied extensively. The purpose of this study is to evaluate the value of MRI in HCM compared by ECG.

MATERIALS AND METHODS

Patients

From October 2002 to April 2003, cardiac MRI was performed in 18 patients with HCM(14 male, 4 female; age range 22-76; mean age 58.5 years) and in 14 healthy volunteers. Asymmetric septal hypertrophy was found in 16 patients and apical hypertrophy in two. Some of these patients experienced pain of chest, palpitation, and arrhythmia. Others had no symptom. The diagnoses of all these patients were based on ECG and clinical findings.

Technique

MR images were acquired with a 1.0T superconductive MR(Impact, Siemens). Conventional non-breath-hold cine MR images obtained in the trans-axial plane by using a spin-echo(SE) sequence. The breath-hold cine MR data were acquired by a fast low angle shot gradient-echo(FLASH) sequence gated electrocardiographically. Gating was performed prospectively by using the R wave as a trigger. A segmented K-spaced data acquired was employed to obtain images of several phases of the cardiac cycle within a single breath-hold. A flip angle of 30°, a section thickness of 8mm, a 30×35 cm field of view, and acquisition matrices of 140 × 256 were employed. To obtain an adequate image of the cardiac chambers, various views were obtained including transverse imaging, the long axis of the left ventricle(LV),

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the four-chamber view and the short axis view of the LV.

Images analysis

The thickness of septum at the basal segment and posterolateral free wall was measured in the LV end diastole by MRI. Some indexes such as Left Ventricular End Diastole Diameter(LVEDD), Left Ventricular End Diastole Volume(LVEDV), and Ejection Fraction(EF) for evaluating cardiac function were measured by using ARGUS auto-quantitative program.

Statistical analysis

t test was used to compare the measurements between the HCM and the healthy volunteers and also between MR and ECG. All data were analyzed by SPSS11.0 statistic software.

RESULTS

The images of LV in different motion period are obtained by the FLASH sequence(***Fig 1***). 16 were classified as having asymmetric septal hypertrophy(***Fig 2***) and two as having apical hypertrophy.

The septum thickness at the basal segment with HCM was thicker than that of the basal segment in the healthy volunteers. While the myocardial thickness at the posterolateral free wall in HCM has no significant difference with that in the healthy volunteers(***Tab 1***).

Other comparisons of MRI vs. ECG measurements of LVEDD, LVEDV, EF were analyzed in 18 patients with HCM shown in ***Tab 2***.

Tab 1 **Mean myocardial thickness in 16 patients with HCM and in 14 healthy volunteers**

	HCM(n = 16)	Healthy Volunteers(n = 14)
Sepal thickness(mm) at basal segment	21.5 ± 5.8	11.4 ± 4.2
Posterolateral wall thickness(mm)	10.3 ± 1.6	11.2 ± 2.1

Tab 2 **This shows comparisons of cardiac function measured by MRI and ECG**

	MRI	ECG	t value	P value*
LVEDD(mm)	47.8 ± 3.5	48.4 ± 4.3	t = 1.15	P > 0.10
LVEDV(ml)	71.1 ± 15.9	75.1 ± 13.7	t = 0.78	P > 0.40
EF(%)	76.6 ± 11.3	64.4 ± 11.8	t = 2.01	P > 0.05

*The differences in value of LVEDD, LVEDV and EF were analyzed statistically between MRI and ECG by using the unpaired Student's *t* test.

DISCUSSION

Clinical features of HCM

The feature of HCM is asymmetric hypertrophy in myocardium that often involves in the anterior or lateral wall of left ventricle and interventricular septum[2-4]. It is different from myocardial hypertrophy caused by hypertension or stenosis of aorta valve. The typical pathological presentation is the increase of myocardial mass, the abnormal hypertrophy of cardiac cell, muscle cell disorganization and the interstitial fibrosis[5-6]. HCM can be found in any age and many in very young patients. On clinical, some of patients with HCM suffered from chest pain, dyspena, palpitation, and arrhythmia. While others hare no symptom before sudden death[7-9]. There are several subtypes in HCM such as septal hypertrophy, diffusive hypertrophy and apical hypertrophy. In our study, most of cases are septal hypertrophy.

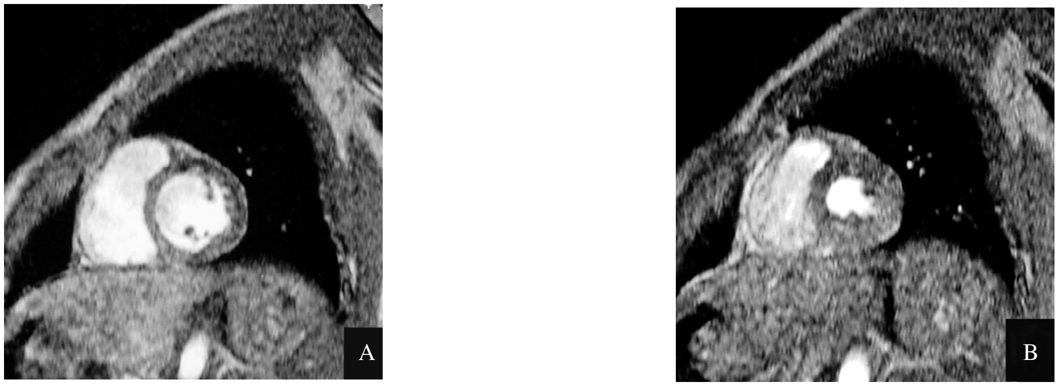
Technique of cardiac MR

MR scan is a kind of method without invasiveness in evaluating the function and structures of cardiac[10]. Nature comparison between the cardinal structures and flowed blood is applied for MR imaging. It can be shown the normal and abnormal cardiac structure and hemodynamical change of cardiac clearly. With the development of MRI, we can not only acquire the anatomy of the part of hypertrophic myocardium, the diameter of atrium or ventricle, and the stenosis of outflow tract of the LV but also calculated the cardiac function such as myocardial mass, end diastole diameter, and ejection fraction[11]. The destination of this study used the breath-hold two-dimension fast low angle shot(FLASH) gradient-echo sequence is to slow down the period of cardiac MR scan[12]. FLASH is a kind of sequence with white blood flowed in the cardial vasculature. The small angle and short repeat time are used in order to get good comparison between the cavity and the myocardium. Conventional cardiac MR needs 1 or 2 hours in the past in one patient. The scan period is shortening greatly by using the FLASH sequence in our study. Furthermore, with the breath-hold cine MR gated electrocardiographically, we obtained the cardiac images not only in end diastole but also in end systole of the LV. After grasping the technique of scan, we need only half an hour to one hour in a patient including data procession.

Comparison of MRI and ECG

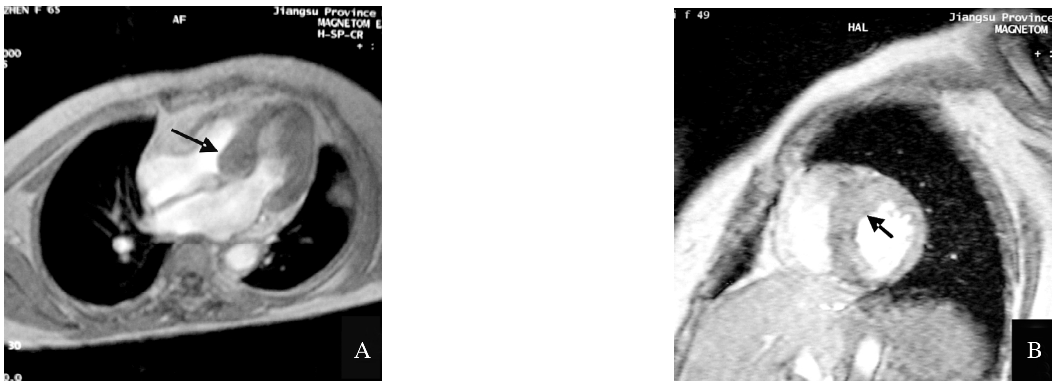
ECG has been widely accepted as a screening study for the diagnosis of HCM and as a definitive diagnostic modality at the same time. The advantages of ECG are much cheaper, more readily available and take less examination time. However, the measurement of cardiac function of ECG comes from the geometrical assumptions. The geometrical assumptions may cause the invalid calculation[13-15].

Compared with ECG, MR has excellent characterization of soft tissue, clear depiction of natural contrast between the blood and cardiovascular structure, good capability of creating images with direct multiple planes. Cardiac MR imaging with electrocardiographic gating sharply delineates the myocardium intensity and the



The end diastole period. The end systolic period.

Fig 1 The LV on short axis in different motion period of cardiac in healthy patients



The hypertrophy of interventricular septum(black arrow) showed on four-chamber view.

The hypertrophy of interventricular septum(black arrow) involved the front wall of LV displayed on short axis.

Fig 2 The hypertrophic myocardium of HCM in different views showed on MRI

high-signal-intensity areas of pericardial fat. Thus, MR imaging in patients with HCM provides useful information about the myocardial hypertrophic distribution and enable the measurement of the wall thickness. Furthermore, the measurements of cardiac function including LVEDV, LVEDD, and EF on the ground of clearly images should be more accurately on theory. In our study, the thickness of the septum and posterolateral wall in the healthy subjects was(11.4 ± 4.2)cm and (11.2 ± 2.1)cm, respectively. These results were similar to those in the other study[16].

While in our study there is no significant agreement between measurements obtained by MRI and ECG at assessment of the cardiac function such as EF, LVEDD and LVEDV. The author thinks the reason of not showing the advantages of MRI in evaluating the cardiac function is the limitation of 1.0T MRI. A lower tesla magnetic intensity of MR confines the display of cardiac anatomy.

Limitation in this study

In the period of breath-hold cine MR, the span of breath-hold time is different from heart rate in every patient. Generally speaking, the fast rate a patient has, the shorter time is needed. While almost all of HCM has slow rate under 70 beats a minute due to administrating Betabloc(metoprolol tartrate)[17], it will need a long time to hold breath in 20 to 30 second, even in 34 second. To some old patients or others with pool function of cardiac, they cannot hold breath in the whole period. In our study, the HCM patients’ respiration must be trained and could be taken easily to ensure obtaining good images. Otherwise, the scan cannot be triggered by the R wave and the images are not clear because of the movement artifact.

In conclusion, MRI can fully provide the abnormalities of cardiac function in HCM; thus, it is of great value in clinical application.

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· *Abstract* ·

Harnessing transposons for cancer gene discovery

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Cancer gene discovery continues to drive current cancer research with the promise of identifying new diagnostic markers and therapeutic targets by elucidating novel genetic interactions that promote or sustain tumor formation. *Sleeping Beauty*(SB) transposon-mediated insertional mutagenesis has emerged as an exciting approach to identify novel cancer-causing genes in the mouse. The SB transposon faithfully "hops" throughout the genome by a cut-and-paste mechanism mediated by the ubiquitous expression of the SB transposase. Initial tumor data generated using an SB transposon harboring the MSCV promoter demonstrated a bias towards hematopoietic tumors. More recently, experiments using a modified SB transposon containing the CAG promoter have generated cohorts of mice with solid tumors, primarily carcinomas, which in some cases metastasize. Many animals also develop multiple, independent primary tumors. These data demonstrate the utility of the SB transposition system for cancer gene discovery across organ systems. Recently, our lab has also developed an inducible expression system for the SB transposase that should allow for saturation mutagenesis in any given tissue of interest in both wild type or sensitized mutation backgrounds. We are currently using this inducible SB transposition system to interrogate the genetic pathways involved in the initiation and progression of several solid tumor types, including skin, liver, GI and pancreas.

Key words: cancer gene; sleeping beauty; hematopoietic tumor