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Original Article

Comparison between magnetocardiography and myocardial perfusion imaging in the diagnosis of myocardial ischemia in patients with coronary artery disease

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Abstract: Objective: Compared the role of Magnetocardiography (MCG) and myocardial perfusion imaging (MPI) in the diagnosis of myocardial ischemia. Methods: Thirty-two patients were diagnosed as coronary artery disease (CAD group) by coronary angiography (CAG), while 72 cases were in non-CAD group. All patients received CAG, MCG, and MPI. Results: Seven parameters of MCG respectively with sensitivity of 50.00%, 36.36% and 62.50%, 50.00%, 53.12%, 71.88%, 25.00%, specificity of 81.94%, 68.06% and 62.50%, 83.33%, 62.50%, 62.50%, 87.50%; MCG7 parameters of any two or more positive, with a sensitivity of 81.25%, specificity of 59.72%, more than any three positive, with a sensitivity of 65.63%, specificity of 69.44%; MPI in diagnosis of coronary heart disease with a sensitivity of 75.00%, specificity of 79.20%. Conclusions: In the diagnosis of myocardial ischemia, MCG and MPI had good value in clinical application.

Keywords: Magnetocardiography, coronary heart disease, myocardial perfusion imaging

Introduction

Magnetocardiography (MCG) is a noninvasive method for the recording of magnetic fields generated by the electrical activity of the heart [1, 2]. Because the recorded signal is generated by tangential direction, the magnetic signal of AC and DC can be simultaneously detected [3]. So that cardiac electrophysiology can be reflected well. The changing of the resting membrane potential, peak amplitude, duration, the upstroke velocity and the propagation velocity of the transmembrane action potential in the myocardial ischemia region causes the propagation direction of the ischemic region and the edge area heterogeneous, which is discrete [4]. ST-segment changes in ECG records can reflect ischemic injury induced current, but require exclusion for abnormal ST segment changes caused by non-ischemia-induced depolarization [5]. At present, the MCG can be used for the early diagnosis of chronic myocardial ischemia, detection of myocardial viability and assessment of the degree of risk of malignant arrhythmias after myocardial infarction, and following up for coronary heart disease patients (including drug therapy, coronary angiography and coronary artery bypass grafting) [6-8].

Coronary artery disease (CAD) is one of the leading causes of death worldwide [9]. In China, although CAD is not as common as in Europe and United States, the morbidity and mortality are gradually increased and even accelerated in recent years [10, 11]. As the most commonly used noninvasive instrument, electrocardiogram (ECG) has high specificity but low sensitivity. However, as the golden standard of diagnosing CAD, coronary angiography is invasive, costly, and suffering [12]. Therefore as a noninvasive, risk- and radiation-free method, Magnetocardiography (MCG) received increasing attention [13]. MCG could detect abnormal cur-

Table 1. Patients characteristics in CAD group and in non-CAD group

	CAD group (n = 32)	non-CAD group (n = 72)	*P* value
Sex (males/females)	22/10	49/23	0.567
Age (years, mean ± SD)	58.56±8.13	54.74±8.58	0.035
Hight (cm, mean ± SD)	167.45±7.99	167.65±8.52	0.914
Weight (kg, mean ± SD)	74.77±12.17	73.49±13.13	0.642
Hypertension (cases)	16	26	0.132
Diabetes (cases)	7	8	0.128
Hyperlipidemia (cases)	2	11	0.169
Smoking (cases)	17	11	0.000

rent flows caused by transient acute myocardial ischemia, which might be useful for detecting tiny myocardial lesions; therefore it could be used for early diagnosis of myocardial ischemia. Studies have shown that MCG in the diagnosis of coronary heart disease has good sensitivity and specificity.

Materials and methods

Patient population

The study included 104 subjects that underwent examination of magnetocardiography (MCG), radionuclide myocardial perfusion imaging (MPI) and coronary angiography (CA) simultaneously for treatment in the hospital and outpatient clinic of TEDA international cardiovascular disease hospital between January 2009 and December 2009. CAD group had 32 patients with narrowing of the coronary arteries ≥ 50% in one or more vessels, among them, 22 males, 10 females, mean age 58.6±8.1 years, range 32~79 years. Non-CAD group had 72 patients without narrow or with narrowing of the coronary arteries < 50%, of them, 49 males, 23 females, mean age 54.7±8.6 years, range 26~77 years. The distribution of sex, age, height, body weight, as well as hypertension, diabetes mellitus, hyperlipidemia, smoking history between the groups is listed in **Table 1**. The inclusion criteria were as follows: i) pathologically diagnosed with magnetocardiography (MCG), radionuclide myocardial perfusion imaging (MPI) and coronary angiography (CA); ii) patients signed informed consent; and iii) patients willing to cooperate with researchers. Exclusion criteria include: (1) serious hypertension (blood pressure > 180/110 mmHg), (2) complex arrhythmias (frequent ventricular premature contraction, ventricular tachycardia and complete bundle branch block), (3) serious pulmonary disease and chest malformation or surgery, (4) < 3 months post-AMI, (5) ventricular hypertrophy or dilated cardiomyopathy confirmed by Echo, (6) valvular heart disease, (7) congenital cardiovascular disease, (8) post pacemaker, (9) heart failure NYHA > class III, (10) dysfunction of liver and kidney as well as abnormal electrolyte. All the patients signed written informed consent. This study was approved by the Ethical Committee of TEDA International Cardiovascular Disease Hospital.

Methods

Magnetocardiography

The magnetocardiographic examination was performed using the 9-channel mapping system "CMI 2409" (CardioMag Imaging Inc., Schenectady, New York, USA) in an unshielded room. MCG system is composed of nine DC-SQUID sensors arranged in a 3 × 3 rectangular grid and separated from each other by 4 cm. Four sequential recordings of a total of 36 points were taken within 20 × 20 cm directly over the precordial area. For the MCG imaging, all magnetic, electronic and metallic objects were removed. Laser point the jugulum, and then MCG recordings were carried out by moving the bed at each position according to patient's height and circumference. Data were recorded sequentially at four pre-defined positions for a total imaging time of 6 min with simultaneous registration of the surface ECG as a reference signal for MCG signal averaging. After that, raw, unfiltered MCG data was stored on hard disk for future evaluation. The MCG data were analyzed in scalar form within T waves. System automatically drew an iso-magnetic map from 36 points of magnetic field component. With this map, 7 quantitative parameters were then calculated. There are abnormal value range of seven parameters (**Table 2**) [14].

Radionuclide myocardial perfusion imaging (MPI)

Imaging acquisition: Exercise stress/rest gated MPI was performed on all patients before or after CTCA. Beta-blockers, calcium channel blockers, and nitrates were discontinued at least 24 h before MPI. The exercise stress tests

Table 2. Abnormal value range of seven parameters

Parameter	Unit	Abnormal value range
Pre-peak repolarization		
Angle (frontal plane)	Degrees	< -120 or > -25
Rajectory	Centimeters	≥ 4.3
Angular deviation	Radians	≥ 0.5
Post-peak repolarization		
Angle (frontal plane)	Degrees	< -110 or > -22
Trjectory	Centimeters	≥ 3.7
Angular deviation	Radians	≥ 0.45
Pre-Post Angle Change	Degrees	< -35 or > -12

Table 3. Standard fourfold table of the diagnostic test parameters

Diagnosis test	Standard diagnosis method	
	Disease	No disease
Positive	True positive[a]	False positive[b]
Negative	False negative[c]	True negative[d]

a: number of patients with disease having a positive test result (true positive). b: number of patients without disease having a positive test result (false positive). c: number of patients with disease having a negative test result (false negative). d: number of patients without disease having a negative test result (true negative). Sensitivity (Sens) = true positive/(true positive + false negative) × 100% = a/(a + c) × 100%. Specificity (Spec) = true negative/(false positive + true negative) × 100% = d/(b + d) × 100%. Accuracy = (true positive + true negative)/(true positive + false positive + false positive + true negative) × 100% = (a + d)/(a + b + c + d) × 100%. Positive predictive value (PPV) = true positive/(true positive + false positive) × 100% = a/(a + b) × 100%. Negative predictive value (NPV) = true negative/(false negative + true negative) × 100% = d/(c + d) × 100%. Positive likelihood ratio = Sensitivity/(1 - specificity) = [a/(a + c)]/[b/(b + d)].

were performed according to a modified Bruce's protocol on a bicycle ergometer with a 12-lead ECG, and blood pressure measurements were taken at the baseline and every 2 min during the whole procedure. The endpoints for the stress tests included any one of the following indexes: reaching target heartbeat [(220-age in years) × 85%], ischemic ST-segment horizontal or downslope depression of ≥ 2 mm, emergence of typical angina, severe cardiac arrhythmia, hypertension (≥ 240/120 mmHg), and a fall of systolic pressure ≥ 40 mmHg. At the peak of exercise, a 925-MBq dose of ^{99m}Tc-MIBI was injected into the bloodstream through the vein, and the patient continued to pedal for an additional 1 min. The ECG and blood pressure were monitored before and throughout the test and again after the injection. The acquisition for stress gated-SPECT study was performed about 1 h after injection. Rest studies started acquisition about 1.5 h after injection by using the same amount of doses. The imaging system was a GE Millenium VG & Hawkeys dual-detector SPECT. The acquisition parameters were listed as follows: a low-energy, high-resolution collimator; a 20% symmetric window at 140 keV; a 64 × 64 matrix; an elliptic orbit with step-and-shoot acquisition at 6° intervals over 180° from the right anterior oblique 45° to left posterior oblique 45°; and 25 s dwell time per stop. Acquisitions were gated at 8 frames per R-R cycle with a 50% window of accepted heart rate.

Image reconstruction and interpretation

All data were transferred to an eNTEGRA workstation and reconstructed without x-ray attenuation correction. Images were reconstructed into short axial, horizontal axial, and vertical long axial sections. SPECT image interpretations were visually performed by two experienced nuclear physicians. Tomographic slices were divided into 17 segments according to the American Heart Association model: four segments in the apex on short axial slices; six segments in the middle of left ventricle on short slices; six segments in the basal short axis; one segment in the apex on vertical long axial slices. Each segment was allocated to coronary artery territories according to the reference.

Statistical method

Normal distribution of measurement data is expressed as mean value ± standard deviation (Mean ± SD). Two groups were compared using t-test; Wilcoxon test was used to compare skewed distribution of measurement data. A *P* value of < 0.05 was considered statistically significant difference. Establish a database in Excel statistics and apply SPSS13.0 statistical package. Calculate the sensitivity, specificity, accuracy, positive predictive value, negative predictive value and positive likelihood ratio. Parameters of diagnostic test parameters are calculated as follows: data obtained by standard diagnostic methods and measured by diagnostic test methods are filled in the standard fourfold table (**Table 3**).

Table 4. MCG parameters statistics between CAD and no CAD group

Parameter	No CAD group (n = 72)			CAD group (n = 32)			*Z*	*P*
	P_{25}	P_{50}	P_{75}	P_{25}	P_{50}	P_{75}		
PA	-66.98	-49.66	-29.64	-60.12	-25.55	35.67	-2.74	0.006
PT	2.38	3.60	5.52	2.71	3.79	5.35	-0.983	0.326
PAD	0.26	0.39	0.64	0.32	0.57	1.13	-1.899	0.058
PoA	-55.05	-45.96	-35.62	-47.79	-30.21	46.71	-2.676	0.007
PoT	2.22	2.92	4.80	2.60	4.14	6.07	-2.176	0.030
PoAD	0.26	0.39	0.56	0.38	0.62	1.01	-3.061	0.002
PPAC	-15.08	-8.10	0.31	-17.52	-4.40	8.87	-0.542	0.588

PA: Pre-peak repolarization angle, PT: Pre-peak repolarization trajectory, PAD: Pre-peak repolarization angular deviation, PoA: Post-peak repolarization angle, PoT: Post-peak repolarization trajectory, PoAD: Post-peak repolarization angular deviation, PPAC: Pre-Post angle change.

Results

MCG parameters statistics between CAD and no CAD group

We assessed clinical value of MCG and MPI on diagnosis of ischemia in patients with coronary artery disease. Among the 7 MCG parameters, four parameters, pre-peak repolarization angle, post-peak repolarization angle, post-peak repolarization trajectory and post-peak repolarisation angular deviation, were highly statistically significant between the CAD and non-CAD group with a *P* value of < 0.05 and < 0.01, ≥ 3 parameters (pre-peak repolarization trajectory, pre-peak repolarization angular deviation, pre-post angle change) were not statistically different between the two groups (see **Table 4**).

Diagnostic value of MCG parameters and value of number of MCG positive parameter on CAD

We also observed the diagnostic value of any parameter of MCG7 parameters and the number of positive MCG parameters on detection of repolarization abnormalities. The results of sensitivity, specificity, accuracy, positive predictive value, negative predictive value and positive likelihood ratio of any parameter of MCG7 parameters and the number of positive MCG parameters are shown in **Tables 5** and **6**. From **Table 7**, we can see that the sensitivity and specificity of MCG7 parameters (PA, PT, PAD, PoA, PoT, PoAD, PPAC) are respectively 50.00%, 36.36%, 62.50%, 50.00%, 53.12%, 71.88%, 25.00% and 81.94%, 68.06%, 62.50%, 83.33%, 62.50%, 62.50%, and 87.50%. When combining MCG7 parameters as the standard for the diagnosis of coronary heart disease, the sensitivity and specificity of ≥ 1 parameters positive were 84.38% and 36.11%, ≥ 2 parameters positive were 81.25% and 59.72%, ≥ 3 parameters positive were 65.63% and 69.44%, ≥ 4 parameters positive were 46.88% and 77.88%, ≥ 5 parameters positive were 37.5% and 81.94%, ≥ 6 parameters positive were 25% and 87.5%, ≥ 7 parameters positive were 9.38% and 95.83%.

Comparison between MPI and MCG setting ≥ 2 and ≥ 3 positive parameters asdiagnostic method

We defined any two positive parameters and any three positive parameters of these 7 MCG parameters as the diagnostic standard of coronary heart disease respectively. There is comparison of diagnostic value between the MCG and MPI methods for detection of coronary heart disease (**Figures 1** and **2**).

The distribution of results of the MCG and MPI diagnostic methods in 32 patients with coronary artery disease

Setting any two or more positive of the 7 MCG parameters as the diagnostic methods, the results was that 26/32 patients of the CAG-positive coronary artery disease group were positive in terms of MCG diagnostic methods including 20 (76.9%) cases positive and 6 (23.1%) cases negative with the MPI diagnostic methods; 24/32 patients were positive in terms of MPI including 20 (83.3%) cases positive and 4 (16.7%) cases negative with MCG method. There is distribution of results of 32 CAD patients with the MCG and MPI diagnostic methods (**Figure 3**).

Due to the continuous ionic current of myocardial cell, cardiac depolarization and repolarization are created, as a result excitement is conducted and rhythmic systole is generated [15].

Table 5. Diagnostic value of MCG parameters on CAD

Parameters	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	Positive likelihood ratio
PA	50.00	81.94	72.12	55.17	78.67	2.77
PT	36.36	68.06	58.95	34.29	70.00	1.14
PAD	62.50	62.50	62.50	42.55	78.95	1.67
PoA	50.00	83.33	73.08	57.14	78.95	3.00
PoT	53.12	62.50	59.62	38.64	75.00	1.42
PoAD	71.88	62.50	65.38	46.00	83.33	1.92
PPAC	25.00	87.50	68.27	47.06	72.41	2.00

Table 6. Diagnostic value of number of MCG positive parameter on CAD

Number of positive parameter	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	Positive likelihood ratio
≥ 1	84.38	36.11	50.96	36.99	84.87	1.32
≥ 2	81.25	59.72	66.35	47.27	87.76	2.02
≥ 3	65.63	69.44	68.27	48.84	81.97	2.15
≥ 4	46.88	77.78	68.27	48.39	76.71	2.11
≥ 5	37.5	81.94	68.27	48	74.68	2.08
≥ 6	25	87.5	68.27	47.06	72.41	2
7	9.38	95.83	69.23	50	70.41	2.25

Table 7. Diagnostic value of MPI in coronary artery disease with ischemia

	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	Positive likelihood ratio
MPI	75.00	79.20	77.88	61.54	87.69	3.6

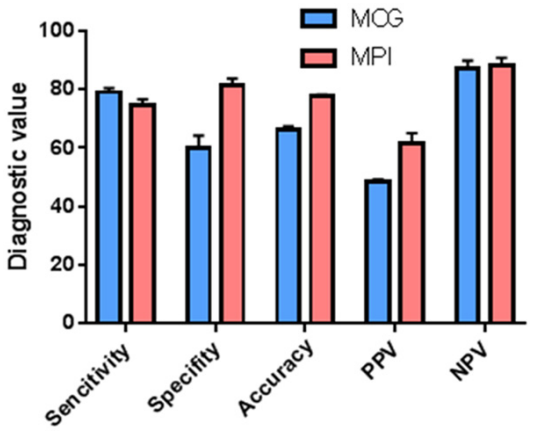

Figure 1. Comparison between MPI and MCG setting ≥ 2 positive parameters as diagnostic method.

The magnetocardiogram (MCG) is an instrument to record and analyze the magnetic fields produced by the ionic currents in the heart [16]. Stenosis or infarction of coronary atherosclerosis, leading to myocardial ischemia and hypoxia, causes myocardial cell metabolism, ion transport and electrophysiological changes. This can lead to sodium ions having abnormally high levels of membrane permeability and accumulated in the cell, and potassium ion leakage to the extracellular membrane, causing low depolarization or part of depolarization in resting stage and creating the conduction of velocity slowing down [17], therefore bring about the nonhomogeneity of myocardial cell repolarization.

Discussion

MCG could make the diagnosis of myocardial ischemia by detecting the change of the ion current. The earliest reports were from Cohen and Kaufman in 1975 [14]. Using MCG they detected the ST-segment changes in the process of making acute myocardial infarction model by dog coronary artery ligation. It suggests the value of MCG in coronary artery disease. But after that MCG was neglected for a long time, until the late 1990s, the value of MCG in coronary artery disease was taken seri-

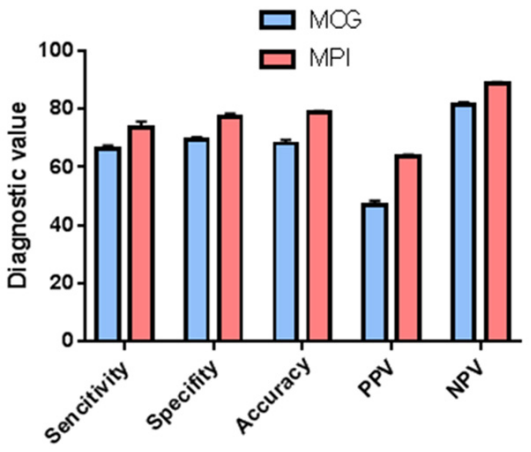

Figure 2. Comparison between MPI and MCG setting ≥ 3 positive parameters as diagnostic method.

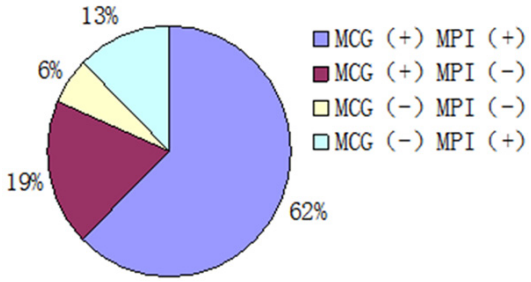

Figure 3. The distribution of results of the MCG and MPI diagnostic methods in 32 patients with coronary artery disease.

ously once again gradually. Despite the lack of clear diagnostic criteria and the support of the gold standard, MCG in the diagnosis of coronary heart disease has showed good sensitivity [18].

In this study, using coronary angiography as the gold standard for diagnosing coronary artery disease, patients were divided into CAG-positive coronary heart disease group and CAG-negative non-coronary heart disease group. We explored the value of the MCG and MPI in the diagnosis of coronary heart disease by MPI as the control study. To our knowledge, there has been no similar report in the country. The author had analyzed the MCG results of 383 cases with CAG-positive coronary heart disease, and 110 cases hospitalized in the same period with CAG-negative non-coronary heart disease, and MCG7 parameters of the two groups showed statistically difference. In this article, compared with the control group only four MCG parameters (PA, PoA, PoT and PoAD) showed significant differences. The inconsistent results may be related to small number of sample cases and the different control group due to different coronary angiography standard (coronary internal diameter reduced < 50%). Our results also show that a single MCG parameter has low sensitivity and specificity for the diagnosis of coronary heart disease. Combining MCG7 parameters, and using ≥ 2 parameters positive as the standard for the diagnosis of coronary heart disease, the sensitivity and specificity were 81.25% and 59.72%, ≥ 3 parameters positive were 65.63% and 69.44%, with the number of MCG parameters positive increased, sensitivity reduced and specificity increased. These results indicate that unlike the morphological diagnosis of coronary angiography, the MCG is more sensitive to the functional changes in regional myocardial ischemia. It follows that the reasons for high false-negative may be that in critical or near critical lesions of coronary artery (stenosis 50% to 70%), coronary autoregulation is not affected, so no significant hemodynamics reduction takes place and myocardial cells have no significant ischemia, therefore the MCG examination showed normal, and it could be confirmed by stress MPI check. Coronary artery spasm or thrombosis due to small plaque rupture and subsequent thrombus autolysis, caused CAG negative, but it has caused the myocardial ischemia, injury and even necrosis of corresponding parts. With the wide application of the CAG, acute myocardial infarction with normal coronary angiography has been reported constantly. As the literature reported [19], 10%-15% patients with myocardial infarction have normal coronary angiography as well as non-coronary arteriosclerosis. In this study, two cases with a history of myocardial infarction, the CAG were negative, but the MPI prompted myocardial perfusion abnormalities, therefore it lead to false positives.

The results showed that the sensitivity of MPI in the diagnosis of coronary heart disease is 75%, specificity 79.20%, positive predictive value 61.54%, negative predictive value 87.69%. Compared with the MCG, ≥ 2 MCG parameters positive as the diagnostic standard of coronary heart disease, sensitivity of MPI is lower than the MCG, but the specificity is higher than the MCG. Tolstrup [20] compared the role of MCG and MPI for the diagnosis of coronary heart dis-

ease, the results showed that the sensitivity of MCG and MPI were 90.1% and 87.5%, the specificity were 68.6% and 75.0%. In this article, 24 patients have positive MPI, and 20 cases of them have positive MCG (83.3%), it also confirmed the consistency of the MPI and MCG in the diagnosis of myocardial ischemia with coronary artery disease. These results indicate that the MCG has good clinical value in the diagnosis of myocardial ischemia with coronary artery disease. It is noteworthy that MPI is a stress myocardial perfusion imaging and the MCG is in the resting state, it indicates that the MCG is superior to the MPI, and stress MCG will increase the positive rates; many exercise or pharmacological stress MCG tests also have confirmed it [21].

The MCG as a noninvasive, risk- and radiation-free method, similar to myocardial perfusion imaging, has better clinical applications value in the diagnosis of ischemia in patients with coronary artery disease [22].

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Disclosure of conflict of interest

None.

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