STRAIGHT LEG RAISING WHILE PERFORMING ^{99m}TECHNETIUM SESTAMIBI INJECTION AT REST CAN REDUCE INFERIOR WALL ARTIFACT IN PATIENTS WITH A LOW-LIKELIHOOD OF CORONARY ARTERY DISEASE

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ABSTRACT

Inferior wall artifacts (IWA) are frequently found in 99mTc sestamibi resting myocardial perfusion imaging (MPI) of a low-likelihood of coronary artery disease patients (LCP). Straight leg raising (SLR) relatively decreases proportion of sestamibi in the liver, so it may reduce subdiaphragmatic activity that can potentially cause IWA. Aim of the study is to investigate whether SLR while performing ^{99m}Tc sestamibi rest injection can reduce the incidence of IWA.

Methods: Incidence of hot and cold IWA were compared between 72 LCP performing SLR during ^{99m}Tc sestamibi rest injection and 125 LCP without SLR. Three inferior segments from 20-segment model were used for myocardial grading.

Results: Age, sex, body weight and stress method for MPI were not significantly different between the two groups. The SLR group had a significantly higher incidence of non-artifact patients compared with the non-SLR group (18.1% versus 4.8%, $P = 0.002$). The SLR group also had a significantly lower incidence of hot IWA. (19.4%vs 41.6%, $P = 0.002$). Incidence of cold IWA were not different between the two groups ($P = 0.225$). Analysis of cold IWA patients showed less severe, even not significantly ($P = 0.085$), different, the same as artifact in the SLR group compared with the non-SLR group.

Conclusion: SLR while performing rest injection can reduce the incidence of hot IWA in LCP and may help in the detection of the lesions in the right coronary artery or left circumflex coronary territories.

Key Words: artifact, coronary artery disease, low-level exercise, technetium-99m sestamibi

INTRODUCTION

Prevention and recognition of an artifact occurring both in the process of image acquisition and processing is of paramount importance to improve the accuracy of myocardial perfusion imaging (MPI) interpretation. Since myocardial perfusion agent such as ^{99m}Tc sestamibi is mainly excreted by hepatobiliary system,[1] therefore hepatic activity and also activity in the gastrointestinal tract can cause artifacts during the MPI processes.[2] This may complicate the interpretation of the inferior wall of the myocardium adjacent

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to these subdiaphragmatic activities.[3]

Low-level exercise has been used in conjunction with pharmacological stress to improve the image quality. Because it can reduce blood flow to the liver and digestive system, resulting in a relatively decreased ^{99m}Tc sestamibi distribution in these organs, therefore it can reduce the inferior wall artifacts.[4-6] Since the artifact seen in patients with a low-likelihood of coronary artery disease (CAD) is likely to be artifactual. In our laboratory, we have observed a significant proportion of a low-likelihood of CAD patients having the inferior wall artifacts on the resting ^{99m}Tc sestamibi myocardial single photon emission computed tomography (SPECT) images. For this reason, we aimed to evaluate whether straight leg raising (SLR) exercise during administration of ^{99m}Tc sestamibi for the resting images can reduce the inferior wall artifacts.

MATERIALS AND METHODS

Patients

This study included two groups of patients referred for rest/stress MPI for the diagnosis of CAD from September 2002 until September 2003, who were categorized as a low-likelihood of CAD. Criteria for low-likelihood of CAD were modified by those of Braunwald E et al.[7] Any patient having any one of the following exclusion criteria was excluded from the study: known CAD; definite angina; probable angina in male older than 60 years or in female older than 70 years; probable angina in patient with diabetes; probable angina in patients with 2 or 3 risk factors including smoking, hypertension and hypercholestero- lemia; hemodynamic change during chest pain; and extracardiac vascular disease.

Patients in the first group (non-SLR) consecutively recruited from September 2002 to April 2003 consisted of 125 patients not performing SLR during administration of ^{99m}Tc sestamibi for the rest study. The second group (SLR) prospectively included 72 nonconsecutive patients from May 2003 to September 2003 who performed SLR while ^{99m}Tc sestamibi was injected for the resting images. Patients who could not do SLR were excluded from the study.

Myocardial perfusion imaging protocol

All patients underwent same-day rest/stress protocol after fasting for at least 6 hours. The rest study was performed first by administration of ^{99m}Tc sestamibi (3.7 MBq per kilogram of body weight) and image acquisition was performed 20-30 minutes later. Three minutes before this injection, a tablet or half a tablet of anginine (600 micrograms of glyceryl trinitrate) was given sublingually to the patient (for body weight > 70 and < 70 kilograms, respectively) who had a history of acute myocardial infarction, coronary artery bypass graft surgery or coronary angioplasty. The stress study began 30 minutes to 2 hours later depending on the availability of the stress laboratory. It was preferably performed by symptom -limited upright bicycle ergometry. At the peak of the exercise, ^{99m}Tc sestamibi (11.1 MBq per kilogram of body weight) was injected and the exercise was continued for further 1 to 2 minutes. The image acquisition was performed about 20 to 30 minutes later. If the exercise was not possible or suboptimal, pharmacologic stress was performed instead with a standard protocol using dipyridamole or dobutamine as appropriate.

Straight leg raising

During lying down on a couch for ^{99m}Tc sestamibi rest injection, patients in the SLR group were asked to raise his/her leg straightly for about 45 degrees, one after the other continuously, beginning one minute before and until two minutes after ^{99m}Tc sestamibi injection.

MPI = Myocardial Perfusion Imaging
CAD = Coronary Arterial Diseases

Myocardial SPECT acquisition, processing and interpretation

The patient was given a cup of water to drink right before the imaging, both in resting and stress studies. Myocardial SPECT was performed with the patient in the prone position for both acquisitions. Three gamma cameras were used in this study, which included MultiSPECT-3 (Siemens, Hoffman Estate, Ill), E-Cam (Siemens, Hoffman Estate, Ill) and Irix (Marconi Medical Systems, Cleveland, OH). Low -energy, general-purpose collimator was used for all cameras and the matrix size was 64 x 64 pixels.

Images were reconstructed after low-pass prefiltering (Butterworth order, 10; cutoff frequencies, 0.45 for resting and 0.4 for stress studies for Multi SPECT-3 and E-Cam, and 0.2 for resting and 0.25 for stress studies for Irix) and ramp-filtered backprojection. No attenuation correction or scattered correction was applied. Transaxial slices were reoriented by a computer program to obtain oblique angle tomograms parallel to the long axis of the left ventricle.

Gated SPECT acquisition was applied only for the stress study. Eight frames per cardiac cycle were used. The reconstructed electrocardiography (ECG) gated SPECT images were processed and displayed by GS-Quant or QGS software.

MPI interpretation was performed by two experienced nuclear medicine physicians. The cine images were reviewed first to detect artifacts in the reconstructed images during image interpretation. Then the tomographic slices of the myocardium in the short axis, vertical long axis and horizontal long axis were evaluated. Wall motion and thickening of the stress study were also reviewed. Normal scan for this study was defined as absence of perfusion abnormali- ties. Abnormal scans were defined when there was reversible defect (ischemia) or fixed defect (infarct).

Inferior wall grading and definition of artifact

The 20-standard segment model was used to evaluate the degree of myocardial uptake.[8] Three of these 20 segments, representing the inferior wall region, were graded visually by using a 5-point scoring system (0, normal uptake; 1, minimally decreased uptake; 2, moderately decreased uptake; 3, severely decreased uptake; 4, absent uptake) by two other observers, with consensus, blinded to relevant clinical data including SLR performed. Non-artifact patient was regarded when all of three segments were graded as 0. Patient was regarded as having the hot artifact if at least one of the three segments had abnormally high uptake precluding accurate uptake grading. Cold artifact was defined in each segment if it was graded as 1, 2, 3 or 4. For patients having the cold artifact, severity of the artifact was further determined from an average grade of the three segments.

Statistical analysis

Continuous data were expressed as mean ± SD if normally distributed, or as median and range if not normally distributed. Categorical data were expressed as percentage. Age, body weight and severity of cold artifact between the two groups were compared by unpaired Student's *t*-test or Mann-Whitney U test, when appropriate. Difference between gender, the incidence of non-artifact, hot artifact and cold artifact cases used were compared using Fisher's exact test. A probability value less than 0.05 was considered to be statistically significant. The power to detect the reduction rate of the incidence of artifact patients between non-SLR and SLR groups was calculated at a significant level of 0.05 from our sample size of 125 for non-SLR group and 72 for SLR group.

RESULTS

Characteristics of patients were shown in Table 1. There were no significant differences between the two groups in terms of age, gender, body weight, stress method for MPI and percentage of abnormal MPI results. Patients with SLR had a significantly higher proportion of smoking ($P = 0.002$) and family history of heart disease ($P = 0.001$) as the risk factors of CAD compared with those in the non-SLR group.

MPI results were positive in 7 patients (5.6%) without SLR (6 ischemia and 1 infarct) and 5 patients (6.9%) with SLR (4 ischemia and 1 infarct). The follow-up to find if coronary angiography was subsequently performed was not possible in one and two scintigraphically abnormal patients in the SLR and non-SLR groups, respectively. Apart from these patients, angiogram was performed in only a patient in the SLR group who had anterolateral ischemia on MPI, and was found to have 80% stenosis of the proximal diagonal branch of the left anterior descending coronary artery. We did not find unpleasant symptoms or adverse effects from the SLR in any patient.

Table 2 compares the incidence of artifacts between the groups. Significantly higher incidence of non-artifact patients was found in the SLR group compared with the non-SLR group (18.1% versus 4.8%, $P = 0.002$). In addition, patients with SLR had a significantly lower incidence of hot artifact compared with those in the non-SLR group (19.4% versus 41.6%, $P = 0.002$). However, the incidence of patients with cold artifact was not significantly different between the groups (53.5% versus 62.5%, $P = 0.225$). In patients with cold artifact, severity of the artifact shown by the mean ± SD (range) of average myocardial uptake grade of the three inferior wall segments was 1.209 ± 0.633 (0.333 -2.333) and 1.000 ± 0.599 (0.333-2.667) in non -SLR group and SLR group, respectively ($P = 0.085$).

TABLE 1 Characteristics of patients.

	Non-SLR (n = 125)	SLR (n = 72)	*P*-value
Age (y)	53.2 + 12.6	50.9 + 10.7	NS
Male gender	55 (44.0)	32 (44.4)	NS
Body weight (kg)	79.8 + 19.0	79.9 + 17.8	NS
Risk factor			
Smoking	16 (12.8)	22 (30.6)	0.002
Hypertension	20 (16.0)	19 (26.4)	NS
Hypercholesterolemia	12 (9.6)	4 (5.6)	NS
Positive family history	26 (20.8)	31 (43.1)	0.001
Stress method			
Upright bicycle ergometry	110 (88.0)	64 (88.9)	NS
Dipyridamole	11 (8.8)	8 (11.1)	NS
Dobutamine	4 (3.2)	0 (0)	NS
Abnormal scan	7 (5.6)	5 (6.9)	NS

SLR, straight leg raising; NS, not significant.
Values presented are mean + SD or number of patients (%).

TABLE 2 Comparison of the incidence of each type of artifact between the two groups.

Incidence*	Non-SLR (n = 125)	SLR (n = 72)	*P*-value
Non-artifact patient	6 (4.8)	13 (18.1)	0.002
Hot artifact patient	52 (41.6)	14 (19.4)	0.002
Cold artifact patient	67 (53.6)	45 (62.5)	NS

SLR, straight leg raising; NS, not significant.
* Values in parenthesis are percentages.

From our sample size in both groups, the power to detect the reduction rate of the incidence of artifact patients from non-SLR (95.2%) to SLR (81.9%) groups was 80% at a significant level of 0.05.

DISCUSSION

^{99m}Tc sestamibi is mainly excreted by hepatobiliary system so subdiaphragmatic activity can be found in the liver, gallbladder, small and large intestine and the stomach, the latter due to duodenogastric reflux.[1] The liver activity is particularly prominent at rest and in pharmacologic stress studies. This intense hepatic activity can interfere with the image interpretation in several ways. First, it can give scattered counts to the adjacent inferior wall, creating a hot artifact, and therefore cause underestimation of perfusion defect in this region. Second, a false defect, or cold artifact, in the inferior wall can occur by oversubtraction of the counts from the inferior wall during image processing. In addition, if the images are normalized to the artifactually high counts in the inferior wall, it can create a false defect to the rest of the myocardium, particularly the anterior wall. This can substantially degrade the image quality and can render images uninterpretable.[9]

In patients with a low-likelihood of CAD, the inferior wall defect is likely to be artifactual either from subdiaphragmatic intense activity or diaphragmatic attenuation particularly in male patients. However, the latter cause may be partly resolved by prone imaging as we routinely use.[10-11] In an attempt to reduce subdiaphragmatic activity, apart from keeping the patient fasting before tracer injection, the easiest way may be increasing the interval between tracer injection and imaging. However, this may limit laboratory efficiency in particular for the busy and space-limited department like ours, where the usual time interval between tracer injection and rest imaging was only about 20-30 minutes.

CAD = Coronary Arterial Disease

Low-level exercise or a change in subject's position can rapidly change hepatic blood flow because portal vein, which supplies approximately 80% of the blood to the liver, is a low-pressure system. In addition, the liver as well as the digestive system can alter their plasma volumes almost instantaneously through sympathetic vasoconstriction, mediated by alpha-adrenergic receptors, in reflex response to the stress. This venous constriction causes displacement of a large volume of blood from the liver to the veins in the thorax.[12] After intravenous injection, ^{99m}Tc sestamibi rapidly clears from the blood pool.[1] SLR, as a low-level exercise, during administration of ^{99m}Tc sestamibi, stimulates sympathetic nervous activity and therefore decreases blood flow to the liver and digestive system, while provides a redistribution of blood flow to the leg muscles under activity. These mechanisms result in a lower proportion of ^{99m}Tc sestamibi localizing in the liver. Combination of a low-level exercise to the pharmacological stress has been shown to improve the image quality and reduction of artifacts caused by hepatic activity.[4-6] We adopted this concept to the rest images by introducing SLR exercise during ^{99m}Tc sestamibi injection.

We found that SLR could significantly decrease the incidence of inferior wall hot artifact patients and increase the proportion of non-artifact patients; hence improve the image quality and accuracy of MPI interpretation. Although SLR did not appear to reduce the incidence of cold artifact in our population, it showed a trend to reduce the severity of the cold artifact in these patients.

Our study had some limitations. Since data from the non-SLR group were retrospectively collected. We had to use the criteria for a low-likelihood for CAD only from the itemized data we had recorded. These were purely based on the clinical history without associated ECG data. However, only about 6% of patients in each group had abnormal MPI results and only one of them was confirmed a significant stenosis by coronary angiography. In addition, it seems reasonable to expect differences in terms of body habitus of these patients between the groups, which can cause inferior wall attenuation artifact from the diaphragm in different degrees.[13] Although we did not have the records about the bra-cup size, size and density of the breast in our female population, and degree of lateral chest wall fat and abdominal protuberance in male subjects,[13] the possible impact of these factors were in part eliminated by the comparable proportion of gender and body weight between the groups and the prone imaging position in our study.

CONCLUSION

We have shown that applying SLR exercise in patients undergoing MPI during ^{99m}Tc sestamibi injection for the rest imaging can reduce the incidence of artifact in the inferior wall of the left ventricular myocardium. Although conducted in the low -likelihood of CAD patients, theoretically it can be generalized to the intermediate and high-likelihood of CAD patients as well. SLR can be incorporated into the protocol for rest injection without difficulty or detrimental effects to the patients. It can reduce the repeated scans and increase the patient throughput of the laboratory. Most importantly, this procedure has a potential to increase the sensitivity in detecting CAD lesions in the right coronary artery and left circumflex coronary artery territories, particularly in patients with multi-vessel disease. Further studies are needed to clarify this issue.

SLR	=	Straight Lig Raising
MPI	=	Myocardial Perfusion Imaging
CAD	=	Coronary Artery Diseases

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