The Effect of a Shortened Fasting State Prior to Radiotracer Administration on Upper Abdominal Artifacts in Myocardial Perfusion Scan: A Pilot Study

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ABSTRACT

Objective: To evaluate the effect of shortened fasting state prior to radiotracer administration on upper abdominal artifacts, study duration, and patient side effects in myocardial perfusion study and to identify any factors that may correlate with the presence of upper abdominal artifacts on imaging.

Methods: Pilot study in twenty eligible patients who underwent myocardial perfusion was done. All patients were instructed to have a light meal between 2-4 hours prior to radiotracer administration, both for rest and stress studies. Other preparation and protocol were performed according to our division's protocol. Visual analysis of myocardial perfusion images were evaluated by two nuclear medicine physicians using raw data images (anterior, LAO45 and left lateral views) and SPECT short axis images. The images were scored from 0-3 regarding the artifacts in liver, gallbladder and intestines. Quantitative analysis was done using mean radioactivity counts in inferior myocardial wall, right lobe of liver, gallbladder and intestines and count ratio between myocardial wall and these organs.

Results: The visual analysis in up to 80% of patients showed no artifact in liver, gallbladder and intestine, while 10% showed some artifacts without disturbing scan interpretation and 10% showed artifacts which could be corrected by reconstruction technique without the needed for re-acquisition. The myocardial-to-intestinal ratio in patients without abdominal artifact tended to be higher than in those with abdominal artifacts in both rest and stress studies. Only one patient had transient dizziness after stress, which was most likely due to side effect from adenosine.

Conclusion: There was neither significant effect on the presence of upper abdominal artifacts nor side effect in the patients who had meal until 2 h prior to radiotracer administration in MPS. Thus, this study can be performed in patients who did not fast as instructed by delaying radiotracer administration to 2 h thereafter. This shortening of fasting period may be considered to reduce patient's discomfort and the risk from prolonged fasting state for several hours.

Keywords: Fasting; myocardial perfusion scan; upper abdominal artifacts (Siriraj Med J 2017;69: 268-275)

INTRODUCTION

Radionuclide myocardial perfusion scan (MPS) is a noninvasive imaging modality for management in patients with coronary artery disease (CAD), because of its usefulness in diagnosis, severity assessment of myocardial ischemia and prognostic classification, all of which are beneficial for planning of patient treatment and follow-up.[1,2]

Approximate 2,200 MPS studies were annually performed in Thailand, and approximately 300 studies were performed in our center. The most common indications for MPS are to diagnose and assess the severity of myocardial ischemia. Tc-99m-labelled methoxyisobutyl isonitrile (Tc-99m MIBI) is the most commonly used radiotracer, which its uptake in myocardium is related to blood flow and mitochondrial activity. However, this tracer is mainly

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excreted via hepatobiliary tract, so the image quality can be interfered with by activity in upper abdominal organs including liver, gallbladder and small intestines.[3] There is evidence that myocardial-to-liver uptake ratio decreases during rest, or during pharmacologic stress using vasodilators, such as adenosine or dipyridamole, which results in interference with assessment of myocardial lesion, especially at inferior and/or inferoseptal wall, causing negative effect on diagnostic accuracy and impact on patient diagnosis and management.[4-5]

Several methods were proposed to reduce upper abdominal artifacts but none of them showed clear efficacy in eradicating their presence. In our center, we use combined techniques to reduce upper abdominal artifacts in MPS study, although some patients still showed significant artifacts and needed to re-scan with further delayed images. The need for prolonged study time related to upper abdominal artifact may be up to 20%, particularly in stress study.[6]

Apart from the problem concerning abdominal artifact, there also exists controversy in patient preparation for MPS study, of which the fasting period prior to study is our main interest. The recommendation by the International Atomic Energy Agency (IAEA) in 2006 suggest that fasting state is required for Tc-99m imaging at rest, except for diabetic patients on insulin or oral hypoglycemic agents[7] without definite period of fasting state or any comment on preparation concerning diet for stress study. The guideline developed by the Society of Nuclear Medicine (SNM) in 2008 suggested that patient should be fasting for at least 4 h before rest and MPS, followed by exercise or pharmacologic stress testing.[8] Another guideline provided by European Association of Nuclear Medicine and European Society of Cardiology in 2005 recommended that heavy meal should be avoided before a stress test without any suggestion regarding fasting.[9]

Basically, we had all patients fast for at least 4 h prior coming for MPS study. For patient's convenience, we performed 1-d rest/stress protocol with 3-hour apart for each study, which resulted in approximately 10-hour fasting period for the whole protocol. This prolonged fasting state may cause patients discomfort and increase the risk in some patients eg. diabetics or elderly. If patient did not fast as instructed, his/her MPS would be cancelled, causing delay in diagnosis, loss of unused radiotracer and effect on patient schedule.

The primary objective of this study was to evaluate the effect of shortened duration of fasting period prior to radiotracer administration on upper abdominal artifacts seen in MPS. We also evaluated which factors might correlate to the upper artifact affecting image interpretation, duration of MPS study, and side effects caused by having meal prior to the study.

MATERIALS AND METHODS

Patient population

We performed a pilot study in 20 adult patients who were scheduled for 1-day protocol rest-stress MPS study from January 2014 through March 2015 at the Division of Nuclear Medicine, Faculty of Medicine Siriraj Hospital. These patients were indicated for MPS for suspected CAD or pre-operative evaluation in asymptomatic, patients at risk for CAD. Patients who were not willing to participate; pregnant, had history of hepatic or intestinal surgery; had hepatobiliary tract or intestinal disease which might affect intestinal function, received any drug affecting intestinal motility within 24 h before the study or those whose fasting was recommended due to reason other than for MPS preparation were excluded from the study. This study was approved by the Institutional Ethics Review Board and all patients gave written consent before enrollment into the study.

All patients were instructed with our standard protocol to 1) withdraw nitrate, beta-blocker and calcium antagonists for 24-48 h prior to the study 2) withdraw bronchodilators and caffeine – containing meal/drink for 24 h prior to the study, and 3) withdraw diabetic drug in the morning of the study date. The intervention of this study recommended all patients to have light meal between 2-4 h prior to each radiotracer injection.

Radiopharmaceutical injection and image acquisition

On the study date, preparation check lists were done before MPS study using 1-day rest/stress imaging protocol with at least 3 hour interval between rest and stress studies. The average dose of Tc-99m MIBI were 8.6 mCi (range 6-11.8 mCi) and 25.54 mCi (range 20.2-30.4 mCi) for rest and stress studies, respectively, All patients were asked to drink 250 ml of soy milk at 20 minutes after each injection. The rest and stress images were acquired 40 minutes after radiotracer injection.

Stress testing protocol

Patients were imaged supine on the gamma camera couch with arms raised. All studies were completed with a 90° - angled dual-head SPECT camera (Infinia Hawkeye; GE Healthcare, Wisconsin, USA) using a low-energy, high-resolution collimator with10% energy window centered on the 140 kev Tc-99m photopeak. SPECT data were acquired for 25 s per projection (30 projections/head; total of 180° of data), gated at 16 frames per cardiac cycle. CT attenuation correction was not available. Projection and reconstructed matrix size for all scans were 64x64 pixels, zoom 1.3x with a pixel size of 6.8x6.8 mm in c-mode. Reconstruction was done on a Xeleris 3.0 workstation (GE Healthcare) with standard filtered back projection method using the uncorrected emission data. Both gated and ungated images were used for evaluation. The FBP images were done with a 10^{th} order Butterworth filter, using cut-off frequency of 0.52 and power of 5.

Data collection and Statistical Analysis

The resulting images were separately analyzed for upper abdominal artifact score in a masked manner by 2 experienced board certified nuclear medicine physicians (T.T. and C.K) using 4 DM-SPECT (Invia Medical Imaging Solutions, Michigan, USA) on the same workstation. Differences in scoring between readers were resolved with consensus. Raw data images in anterior, LAO 45° and left lateral views as well as SPECT short axis images were included in visual assessment (Fig 1) and determined using 4-point scale scoring system (modified from Grüning, *et al*[10]) regarding the radioactivity in liver, gallbladder and intestine as follows ; score 0 – no upper abdominal artifact, score 1 – presence of radioactivity adjacent to myocardium without interfering with interpretation; score 2 – presence of interfering activity from upper abdominal organs which was still fixable by pixel truncation technique, without the need for re-scanning; and score 3 – significant interfering activity from upper abdominal organs, which was non-diagnostic without re-scanning.

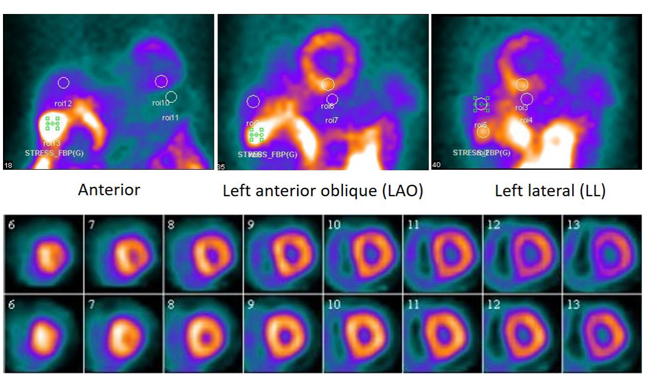

Fig 1. Raw data images of myocardial perfusion scan in anterior, LAO and left lateral views (top row, from left to right) and SPECT short axis images (bottom row) used in qualitative assessment of upper abdominal artifact. The regions of interest (ROIs) used in measuring the mean count activity at inferior wall, right hepatic lobe, gallbladder and intestinal loop adjacent to myocardium obtained from each view and then calculating the activity ratio between myocardium and the rest organs (modified from Grüning,et al[10], Boz, et al[11] and Hara, et al.[12])

One experienced technician (P.M.) performed quantitative analysis by placing 10-pixel sized, circular-shaped ROIs, over inferior wall of left ventricle, right hepatic lobe, gallbladder and upper abdomen just inferior to inferior wall of LV, in anterior, LAO and LLL views, in order to obtain myocardial, liver, gallbladder and intestinal activities, respectively. (Fig 2). The average count activities obtained from these ROIs were used for statistical analysis. The ratio between mean activity in LV and other regions were then calculated.

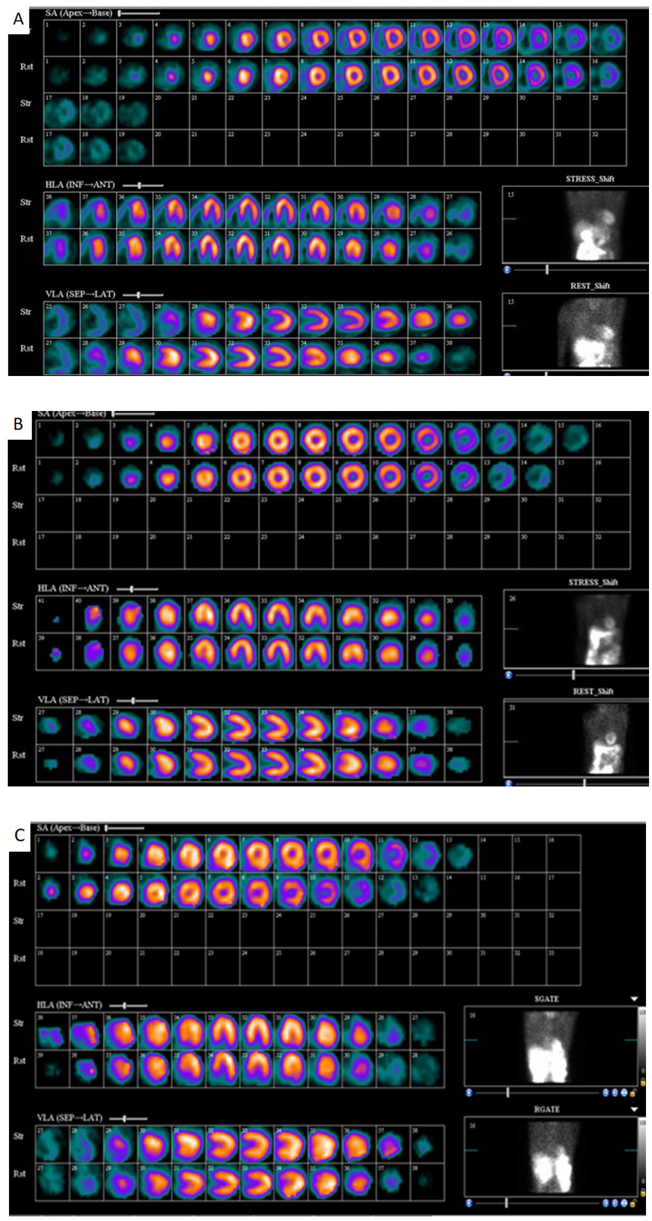

Fig 2. Upper abdominal artifacts score using visual assessment from 0 = no artifact (A), 1 = some artifacts without disturbing interpretation (B) and 2 = significant artifacts needed technical correction (C). None of 20 subjects in this study showed artifacts score 3.

Statistical analysis

The qualitative and quantitative data were analyzed using descriptive analysis, presented as mean (SD), or median (range) for continuous variables and percentages for categorical variables. Continuous variables were analyzed using independent t-test or Mann-Whitney µ test. Categorical variables were analyzed using Chi-square test or Fisher's exact test. Differences were considered to be statistically significant at $P \leq 0.05$. The inter-rater agreement of upper abdominal artifact between two NM physicians was evaluated using quadratic weighted Kappa.

RESULTS

There were 55% female and 45% male, most of them were aged over 65 years, with mean age of 66.9 years (SD 13.38). Most patients had normal to high BMI. The most common indication for MPS study was to diagnose CAD in patients with risk factors. The characteristics of all patients were shown in Table 1.

The duration between meal and radiotracer injection, uptake period, administered radioactivity dose, mean count activity in each region and ratio between count activity in myocardium and other organs in both rest and stress studies were shown in Table 2. All meals were self-provided and all patients had meal prior to their arrival at the department, so other details of meal, such as calories and content were not available

There were approximately 80% of patients who had no artifact to interfere with the MPS image interpretation (score 0), while 10% of patients had minor, insignificant artifact without the need of any intervention (score 1), and only 10% of patients had artifact that was correctable using pixel truncation technique (score 2). (Fig 2) The percentage of these scores were similar between rest and stress studies and none of these MPS images showed significant artifact needed for delayed, re-scanning. (Table 3)

There was very high inter-rater agreement between two physicians with weighted Kappa of 0.85 (SD 0.09,

TABLE 1. Characteristics of the study population (n=20).

	Number	%
Gender:		
Male	9	45
Female	11	55
Age (year):		
Mean (SD) = 66.9 (13.38)		
< 55	2	10
55-65	5	25
> 65	13	65
BMI:		
Mean (SD) = 24.15 (5.63)		
<19	3	15
19-25	9	45
>25	8	40
Indication:		
CAD	16	80
Pre-operation	4	20
Meal:		
Bread	1	5
Congee	5	25
Portridge	10	50
Rice	4	20

TABLE 2. Details of myocardial perfusion scan of study population

	Mean	SD	Minimum	Maximum
Interval between meal and radiotracer injection				
Rest (min)	137.40	29.98	70	195
Stress (min)	131.30	13.93	102	160
Interval between radiotracer injection and scan				
Rest (min)	44.40	8.70	35	69
Stress (min)	42.20	7.36	30	64
Radioactivity				
Rest (mCi)	8.60	1.59	6.00	11.80
Stress (mCi)	25.54	3.07	20.20	30.40
Average myocardial activity				
Rest (count)	71.30	23.92	5.25	123.84
Stress (count)	243.65	77.29	93.73	448.61
Average liver activity				
Rest (count)	57.76	23.04	4.96	96.76
Stress (count)	174.53	77.55	70.78	378.35
Average gallbladder activity				
Rest (count)	110.69	76.29	18.03	362.41
Stress (count)	363.71	213.76	68.18	966.80
Average intestinal activity				
Rest (count)	51.44	19.76	3.04	99.11
Stress (count)	165.72	51.89	109.08	285.39
Myocardial-to-liver Ratio				
Rest	1.33	0.58	.85	3.61
Stress	1.54	0.65	.72	3.91
Myocardial-to-gallbladder Ratio				
Rest	0.80	0.44	.21	1.77
Stress (count)	0.88	0.58	.22	2.52
Myocardial-to-intestinal Ratio				
Rest (count)	1.46	0.40	.69	2.30
Stress (count)	1.50	0.38	.82	2.40

TABLE 3. Percentage of upper abdominal score results from all patients and correlation between upper abdominal score and myocardium-to-intestinal ratio during rest and stress studies.

Abdominal score rest	N (%)	Median	Minimum	Maximum
0	16 (80)	1.49	0.98	2.30
1	2 (10)	1.11	0.97	1.25
2	2 (10)	1.20	0.69	1.73
Total	20 (100)	1.43	0.69	2.30
Abdominal score stress	**N (%)**	**Median**	**Minimum**	**Maximum**
0	15 (75)	1.64	1.20	2.40
1	3 (15)	1.14	0.82	1.30
2	2 (10)	1.02	0.98	1.07
Total	20 (100)	1.53	0.82	2.40

95%CI = 0.65-1.00). The ratio between count activity in myocardium and intestines in patients without artifact (score 0) tended to be higher than in patients with artifact in both rest (score 1 and 2, respectively) and stress studies, particularly during stress. (Table 3)

DISCUSSION

Scattered activity from the organs adjacent to the heart, including liver and intestines, can interfere with both visual and quantitative interpretations and cause artifacts to the reconstructed MPS SPECT images, particularly at inferior and inferoseptal wall of LV. These artifacts are most commonly found during rest or pharmacologic stress studies and also seen more frequently in women, In our study, similar results were found regarding gender difference (score 0 = 82% and 100% , score 1 = 18% and 0% in women and men, respectively), but the same proportions of artifacts were found in both rest and stress studies.

We found only 2 patients (10%) with significant upper abdominal artifact causing interference in the interpretation. Several methods have been proposed to reduce upper abdominal artifacts, for example; ingestion of different kinds of solid or liquid diets after radiopharmaceutical administration, in order to increase intestinal motility and move out from the scanning field[13-15]; distend stomach for pushing down the intestinal loops outside the scanning field[11]; administration of drugs which stimulate intestinal motility[6,16]; oral administration of contrast media to absorb the emitted gamma-rays from intestines[17]; delayed acquisition time[18-19]; positioning[20]; and using new image analysis and reconstruction techniques[10,21] with different success rates. In our center, we use combined techniques including 1) drinking soy milk after radiotracer injection, to stimulate cholecystokinin excretion which resulted in accelerating radiotracer excretion via hepatobiliary tract and to increase intestinal motility, which resulted in reducing accumulation in intestinal loops[22]; 2) ECG-gated acquisition and display in cine mode to assist differentiation between true perfusion defect versus false positive defect caused by artifacts[1]; 3) pixel truncation technique to select the ROI limited to only myocardium with least possible artifact involved[12]; and 4) delayed uptake period to 40-45 minutes starting after tracer injection, a period which showed less intestinal activity as compared to a 15-minute uptake period.[15] The use of combined methods may explain our relatively low rate of artifacts, of which 10% needed further reconstruction and 0% need re-scanning as compared to 20% in the previous study.[23]

There were two female patients who had score 2 – artifact, aged 62 and 74 years with small body build (BMI=16.65 kg/$m^2$and 15.43 kg/m^2, respectively). The characteristics and study parameters in both patients were not different from patients without significant artifact. However, we could use further pixel truncation technique to include only LV wall in the ROI and exclude adjacent interfering activity as much as possible, so the images could be interpreted without the need for re-scanning. We could not analyze which factor might correlate with the presence of artifact due to small number of cases.

The inter-rater agreement of upper abdominal score between two nuclear medicine physicians was highly correlated. The myocardial-to-intestinal ratio tended to decrease in patients with higher score in both rest and stress studies, which reflected good correlation between visual and quantitative assessment, although the statistical significance could not be analyzed due to small sample size.

We evaluated 4 patients whose myocardial-to-liver ratios were less than 1 (2 during rest study, 1 during stress and 1 during both studies), and 3 patients whose myocardial-to-intestinal ratios were less that 1 (1 during rest and 2 during both studies). Of these 7 patients, only two showed significant artifact. Lower myocardial activity may be caused by the attenuation effect from diaphragm or true myocardial perfusion defect. All these 7 patients had negative adenosine test results, 2 of them had fixed defect and 1 had partial reversible defect at inferior wall. During mean follow-up period of 27.7 months (SD 7.39, range 15-35 months), 4 patients showed cardiac event (2 had perfusion defect) while the other 3 patients (1 ischemia and 1 infarct at other walls and 1 negative MPS) remained asymptomatic.

The myocardial-to-gallbladder ratio was not analyzed because gallbladder activity only reflected physiologic excretion of TC-99m MIBI and its location was quite far from LV, so negative effect on image interpretation was not predicted regardless of its high radioactivity.

Only 1 patient reported mild dizziness after stress study, which was more likely associated with side effects of adenosine rather than from having meal prior to the study. Other possible symptoms including abdominal discomfort, nausea or vomiting were not observed. However, all of our patients received adenosine during pharmacologic stress testing, so these results cannot directly apply to those who are planned for exercise stress test until more data is available.

This study has several limitations. Since this was a pilot study to assess the risk of this intervention, it explains why small number of patients were included. Another limitation of this study was relatively prolonged recruitment period, which can be explained by some patients refused to participate after being informed about the chance of re-scheduling or after discussing with their relatives at home. Also because there might be a chance for re-scheduling, we screened eligible cases from only those who lived in Bangkok or nearby provinces. Furthermore, the fasting period in this study was different from the department's protocol, so we agreed to perform this study only when either one of our two doctors were responsible for MPS. These reasons may cause potential selection bias. Moreover, the details of meal, especially the amount of lipid were missing. Thus, we could not evaluate the effect of meal on the presence of interfering radioactivity in the intestine. Finally, the reproducibility of count activity measurement was not available because this step was done only once per each ROI by a single experienced technologist. Hence, we plan to conduct reproducibility assessment in our future research with larger number of patients.

CONCLUSION

Shortening of fasting state in MPS to 2 h prior to radiotracer injection showed neither significant upper abdominal artifact nor side effect in the patients. This study can still be performed in patient who do not fast as instructed, by delaying the radiotracer injection to 2 h thereafter. Revision of patient preparation by shortening fasting period to 2 h before each injection may also reduce patient's discomfort and the risk from prolonged fasting, particularly in high risk patients.

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Conflicts of Interest: None

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