ORIGINAL ARTICLE

Differences in Perfusion between Pharmacological Stress and Exercise Stress on Prone Myocardial SPECT

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Abstract

***Backgrounds*: Myocardial single-photon emission computerized tomography (SPECT) with the patient in the prone position has recently been applied to improve the percentage uptake (%uptake) in the inferior wall by reducing diaphragmatic attenuation. We hypothesized that the type of stress might cause a difference in the %uptake improvement in inferior regions in the prone position. The purpose of this study was to compare the %uptake improvement between exercise and pharmacological vasodilator stress in prone myocardial SPECT.**

***Methods*: Following a SPECT study in the supine position, a second SPECT study was performed in the prone position. The cases of 41 patients were studied prospectively: 21 patients with pharmacological stress and 20 with exercise stress. A segmental %uptake based on the quantification of a polar map was used. Liver and heart average counts were measured with a supine planar image. The correlation between the liver-to-heart ratio and the %uptake increase in the inferior wall was then examined.**

***Results*: Pharmacological stress showed a significantly higher average %uptake increase in the inferior wall compared to exercise stress (5.59±2.86% vs. 3.18±1.84%, p<0.05). The average liver-to-heart ratio was significantly higher in pharmacological than in exercise stress (1.04±0.40% vs. 0.72±0.22%, p<0.01). As the liver-to-heart ratio increased, the %uptake increase in the inferior wall increased (y=5.54x -0.51, r=0.74; p<0.05).**

***Conclusions*: Pharmacological stress in the prone position showed greater increase in the %uptake in the inferior wall compared to the exercise-stress patients, mainly due to the higher liver uptake in the former group.**

Keywords: Attenuation, Coronary Artery Disease, Myocardial Perfusion, Prone Position, SPECT

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Nuclear cardiology procedures play a key role in diagnosing cardiovascular disease, which is so essential to treatment planning. ^{99m}Tc -sestamibi and ^{99m}Tc- tetrofosmin are the radiotracers most commonly used in myocardial perfusion imaging. However, whereas myocardial single-photon emission computerized tomography (SPECT) is a valuable diagnostic tool, there are several artifacts that can limit its utility (1, 2). Photon attenuation by the patient's diaphragm and liver is responsible for one of the most prevalent artifacts in myocardial SPECT.

SPECT imaging in the prone position has been shown to greatly improve the inferior wall counts (3), and therefore combined supine and prone myocardial perfusion SPECT provides a practical means of reducing the false-positive rate associated with supine myocardial perfusion SPECT (4, 5). This is because both the liver and diaphragm move caudally in the prone position relative to the supine position, and the effect of diaphragmatic attenuation is reduced (6). Compared to exercise stress, pharmacological stress has shown a high liver uptake of ^{99m}Tc perfusion radiopharmaceuticals (7, 8). Such

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Table 1 Summary of patient data and their backgrounds

	Pharmacological stress (n=21)	Exercise stress (n=20)	p-value
Age	74.5 ± 13.4	72.9 ± 9.3	ns
Sex (male: Famale)	18:3	18:2	
Body mass index (BMI)	25.0 ± 4.1	24.2 ± 3.4	ns
Hypertension	12	9	
Hyperlipydemia	8	7	
Diabetes mellitus	6	7	
Ischemic heart disease	12	12	
Old myocardial infarction	0	0	

high liver uptake may create artifactual defects in the inferior wall with filtered back-projection reconstruction (9-12). We hypothesized that pharmacological and exercise stress may show different improvements in the inferior wall in a prone SPECT study. The purpose of the present study was to compare relative myocardial perfusion in patients with pharmacological stress and exercise stress using prone myocardial SPECT.

Materials and methods

Patients

We prospectively analyzed the cases of 41 patients who were suspected of having coronary artery disease (CAD), including 21 with pharmacological stress and 20 subjects with exercise stress. In the pharmacological stress group, 12 of the 21 patients had known CAD (Table 1). No patients had evidence of prior myocardial infarction in this group. In the exercise stress group, 12 of the 20 patients had known CAD, and no patients had evidence of a prior myocardial infarction. Patients with an apparent perfusion defect in the inferior wall and cardiac dilatation were excluded. All study participants provided informed consent, ant the study design was approved by the doctors in Hokkaido Cardiovascular Hospital.

Stress test

Pharmacological stress was performed with a dipyridamole (Nippon Boehringer Ingelheim Co., Tokyo) infusion protocol using the standard dosage and timing for the medication (0.14 mg/kg for 4 minutes). Two minutes after the infusion ended, 259 MBq of ^{99m}Tc-tetrofosmin (Nihon Medi-Physics Co., Tokyo) was injected (13). Exercise stress was performed according to the maximal Bruce treadmill protocol. After subjects achieved at least 85% of their predicted heart rate or did not achieve it because of fatigue, chest pain or ECG change, 259 MBq of ^{99m}Tc-tetrofosmin was injected and subjects continued to exercise for 1 minute longer (14).

Acquisition and reconstruction

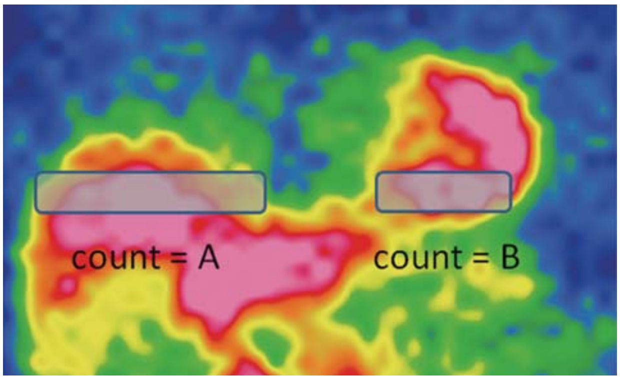
An L-shaped, dual-head gamma camera (GE Medical Systems, Milwaukee, WI) equipped with low-energy, high-resolution collimators was rotated in a 90° arc in a circular orbit from the 45° right anterior oblique to the 45° left posterior oblique positions in a 64 × 64 matrix in 6° steps. The energy window was set at 140 keV ± 10%. After a 60-mine stress test, the first scan was acquired with the patient in the supine position with a step time of 50 sec/step (15). Immediately afterwards, a second scan was acquired in the prone position with a step time of 50 sec/step. Therefore, the total time for the supine and prone SPECT acquisition was 30 min. The direction of the orbit was always right anterior oblique to left posterior oblique relative to the patient, regardless of whether the patient was prone or supine (16).

Projection data were processed using the Xeleraris (GE). The data were pre-processed with a Butterworth filter (order, 10.0; cut-off, 0.40 cycles/cm) (17). A filtered back-projection (FBP) algorithm with a ramp filter was used, and no attenuation or scatter correction was applied.

Analysis

An automatic segmental %uptake measuring method based on quantification of the polar map (Heart Score View, Nihon Medi-Physics Co., Tokyo) was used (18). The regional %uptake values were plotted on a polar map of both supine and prone images (19). We focused on the %uptake in the inferior wall and defined"%uptake increase in inferior wall"as the %uptake in the inferior wall in the prone position minus the %uptake in the inferior wall in the supine position (20).

We selected an anterior planar image in the supine position and set rectangular ROIs (region of interest) to include the target (liver and myocardium) organs (Fig. 1) (21). The lower edge of the myocardium ROI accorded with an epicardial surface in the inferior wall and the height of ROIs accorded with the width of the myocardium in the inferior wall. The "liver-to-heart ratio"was calculated by dividing the liver ROI average counts by the myocardium ROI average counts (22). The correlation between the liver-to-heart ratio and %uptake difference was plotted.



Liver heart ratio
Liver count per pixel / Heart count per pixel = A / B

Fig. 1 Anterior planar technetium (^{99m}Tc) tetrofosmin image used to calculate the liver-to-heart ratio.

Table 2 The %uptake in all segments in supine and prone position

	Supine	Prone	p-value
Anterior	83.3 ± 4.9	79.9 ± 4.9	p<0.01
Septal	73.9 ± 6.5	74.4 ± 5.4	ns
Inferior	72.4 ± 5.1	76.8 ± 4.6	p<0.01
Lateral	83.1 ± 4.4	83.3 ± 4.8	ns
Apex	79.5 ± 6.1	80.2 ± 7.1	ns

Statistical analysis

Results were expressed as the mean ± SD. Statistical analyses were performed using Student's t-test to compare the means of continuous variables and Pearson's correlation test to measure the linear correlation between liver-to-heart ratio and %uptake difference. A p-value of <0.05 was considered to indicate a significant difference. Statistical computations were performed using SPSS (SPSS Inc., Chicago, IL).

Results

Comparison between supine and prone imaging

The %uptake in the inferior wall in the prone position was significantly higher (76. 8 ± 4. 6%) than that in the supine position (72. 4 ± 5. 1%, p < 0. 01; Fig. 2). There was no significant difference on %uptake in the inferior wall between male (4.70 ± 2.74%) and female (3.43 ± 2.15%). The %uptake in the anterior wall in the prone position was significantly lower (79.9 ± 4.9%) than in the supine position (83.3 ± 4.9%, p<0.01). In the other legions, septal, apex and lateral wall, the %uptake in the prone position was not significantly different from that in the supine position (Table 2).

Comparison between pharmacological stress and exercise stress

The uptake increase in the inferior wall with prone SPECT was much greater in the patients with pharmacological stress compared to those with exercise stress. The %uptake increase in the inferior wall was significantly higher for the pharmacological stress (5.59 ± 2.86%) than for the exercise stress (3.18 ± 1.84%, p<0.05; Fig. 3). Fig. 4 shows the liver-to-heart ratio in two different stress studies. The pharmacological stress showed significantly higher liver-to-heart ratios (1.04 ± 0.40%) compared to the exercise stress (0.72 ± 0.22%, p<0.01). When the liver-to-heart ratio was compared with the %uptake increase in the inferior wall, a significant positive correlation between the two parameters was recognized (Fig. 5). As the liver-to-heart ratio increased, the %uptake increase in the inferior wall increased (y=5.54x -0.51, r=0.74, p,0.05).

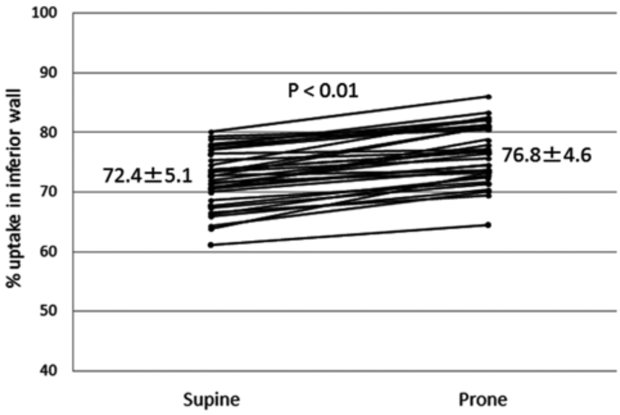


Fig. 2 The %uptake values in inferior wall with supine and prone position.

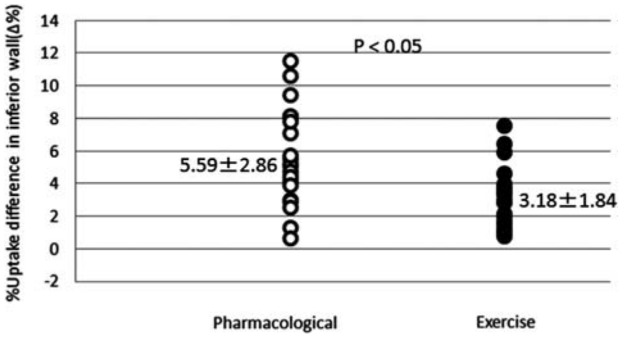


Fig. 3 The %uptake increased in the inferior wall with the prone position with pharmacological stress and exercise stress.

Discussion

The results of the present study confirmed that prone SPECT increased the %uptake in the inferior wall compared to supine SPECT. This improvement in the prone position was significantly greater in the patients who were subjected to pharmacological stress compared to those subjected to exercise stress. Such improvement was closely correlated with high liver uptake. To our knowledge, this is the first report showing the differences of improvement of inferior wall uptake in the prone position between pharmacological stress and exercise stress, and its correlation with liver activity.

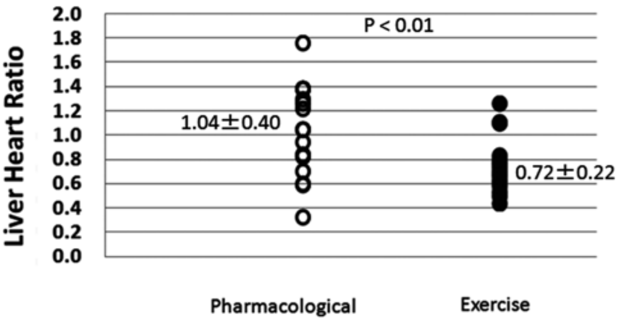


Fig. 4 Liver-to-heart ratios in the supine position with pharmacological stress and exercise stress.

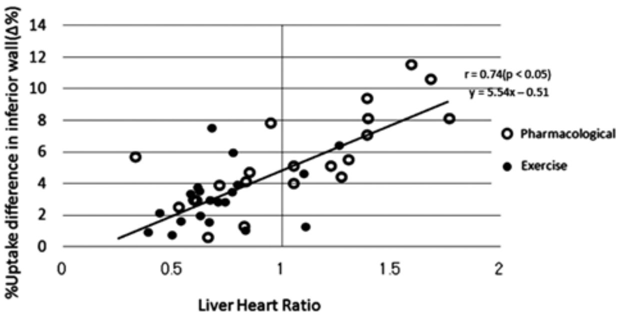


Fig. 5 The correlation between the liver-to-heart ratio and the %uptake increase in inferior wall with pharmacological stress and exercise stress.

Supine versus Prone

The %uptake in the inferior wall was significantly higher in the prone position compared to that in the supine position. Perfusion in the inferior wall was underestimated due to liver and diaphragm attenuation. Ball et al. reported that prone positioning produced a ventral shift of the heart and caudal shift of both the liver and spleen (6). Such organ shifts reduced the overlap of the heart and liver. Consequently, the attenuation of liver and diaphragm was reduced in prone position. There was no significant difference on %uptake in the inferior wall between male and female. In this study, the number of female patients was few and 4 of 5 patients performed pharmacological stress.

The %uptake in the anterior wall was significantly lower in the prone position compared to that in the supine position. This was because the prone position acquisition may produce attenuation artifact in anterior wall due to the closer position of the heart to the sternum bone (23).

Pharmacological versus exercise stress

Regarding the finding that the %uptake in the inferior wall was significantly higher in the patients with pharmacological stress, it should be noted that this was not only because the diaphragm moved caudally but also because the high liver uptake induced a defect of the inferior wall. In the present study, the liver uptake of ^{99m}Tc was higher in the pharmacological-stress group than in the exercise-stress group. This was consistent with the findings of the previous reports (7, 24-26). This was because exercise stress induced an enhanced uptake and longer-term retention in muscle as a result of the increased blood flow, especially to skeletal muscle. Exercise promotes a redistribution of blood flow, shunting it to the skeletal musculature and away from intra-abdominal organs such as the liver (27).

FBP algorithm attempts to limit the star artifact that arises from a superposition of back-projections of the data from the multiple angle acquisitions of a SPECT study. FBP uses a ramp filter; in the spatial domain, this is represented by a decaying oscillation function such that a negative weighting is applied at short distances away from a hot object. This results in decreased activity adjacent to hot objects. The measurement of this activity is called the negative pixel value (28-30). A number of filters such as Butterworth filter applied for FBP may decrease activity adjacent to hot objects persist. Thus, the reconstruction of FBP generates a negative pixel value near the liver, resulting in a reduced count in the myocardial inferior wall (9-12). With respect to the influence on myocardial counts from hot liver activity, the artifactual decrease in inferior activity is worse seems to be greater in higher liver activity. A correlation was observed between the liver-to-heart ratio and %uptake increase in the inferior wall as shown in Fig. 5. Therefore, prone imaging may be effective not only by reducing diaphragmatic attenuation artifacts but also by suppressing the negative pixel value of high liver uptake. A different reconstruction method, such as the ordered subset expectation maximization (OSEM) algorithm, may possibly reduce artifacts from high liver activity (31, 32). Attenuation correction may also reduce such artifacts (33).

Study limitations

There are a number of limitations in the present study. It took relatively long time to acquire both supine and prone images. A long acquisition time tend to cause motion artifact. Recently, SPECT scanners with semiconductor detectors were introduced. The physical performances of these scanners are higher than those of conventional Anger cameras. Especially, high detection sensitivity would solve the problem to require a long acquisition time. Miyagawa had reported that the image acquisition times were 8 and 5 minutes (stress and rest) compared to 15 minutes for each when using conventional SPECT (34). The number of patients was limited (n=41), so that we could not assess the diagnostic accuracy of the present methods. We included those with and without known CAD in order to see the general tendency of tracer uptake. But we eliminated those with evidence of myocardial infarction or those showing large perfusion abnormality in inferior wall. It would be valuable to assess whether the diagnostic accuracy can be improved using a suitable normal database with pharmacological and exercise stress separately. In order to perform such study many more patient data should be collected and compared to the coronary angiographic findings. Further studies using more patient data are warranted in this respect.

Conclusion

Although prone-position SPECT increased the uptake in inferior regions in both the pharmacological- and exercise-stress conditions, pharmacological stress resulted in a significantly higher improvement in inferior wall uptake compared to exercise stress, mainly due to the higher liver uptake in the former.

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Conflicts of interest

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