

# Role of Prone SPECT Myocardial Perfusion Imaging in Patients with Equivocal or Abnormal Supine Myocardial Perfusion SPECT

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## Abstract

Combined supine prone Myocardial Perfusion SPECT (MPS) has been shown to reduce attenuation artifact in comparison to supine only MPS in mixed gender populations with varying risk for coronary artery disease. The aim of this study is to determine whether the additional prone MPS has an advantage over the supine only MPS in determining the diagnostic value of myocardial perfusion SPECT inpatient with known and unknown coronary artery disease.

**Material and methods:** This prospective study was performed on 93 patients, divided into two major groups: patients with known coronary artery disease and without known coronary artery disease. The duration of this study was 06 months including 03 months for clinical follow up. All patients who were assessed using standard stress supine protocol in addition to stress prone included who were observed either inferior, anterior or antero-septal wall perfusion defect in the stress supine study and they were underwent stress prone using LHC as gold standard evaluating coronary artery disease.

**Results:** Total n=93 patients were enrolled in this prospective study and divided into two main categories. Group I (n=29) included 31% of study population with known coronary artery disease and group II (n=64) comprises of 69% of study population with no prior history of coronary artery disease. *Chi-Square* (Pearson) test was applied collectively on both group I and II for statistical analysis which revealed p value of "0.005". Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of prone stress MPS in group I was calculated as 92%, 80%, 96%, 67% and 90% while in group II these values were 86%, 81%, 80%, 87% and 83.3% respectively. The combined sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of prone stress was 89.5%, 81%, 89.5%, 81% and 86.4%.

**Conclusion:** It is concluded that the addition of prone MPS with supine MPS overcomes soft tissue attenuation artifact hence decreases the false positive rates and preventing unnecessary further investigations and improves diagnostic accuracy.

**Keywords:** Prone imaging • Myocardial perfusion SPECT • Coronary angiography

## Introduction

Myocardial perfusion imaging has become an effective clinical tool for diagnosing Coronary Artery Disease (CAD), risk stratifying of patients after infarction, assessing myocardial viability and planning therapy and is usually performed with the patient in the supine position. It is, however, recognized that the diaphragmatic attenuation of the inferior wall and the breast attenuation of the anterior wall in females, has an impact on the test specificity. Planar acquisition, prone imaging, ECG gating and image quantitation constitute overcome soft tissue

attenuation [1]. In the presence of an inferior wall perfusion defect in the stress supine study, positional change (prone imaging) is a low cost, effective and clinically validated technique to overcome soft tissue attenuation artifacts including both diaphragmatic and breast attenuation artifact and helps in accurate diagnosis of coronary artery disease [2]. The purpose of this study is initially to confirm the impact of the supine and prone approaches on attenuation artifacts. Additionally, we investigated its role in reducing subsequent rest imaging and unnecessary referrals to coronary arteriography, aiming to decrease investigation and

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hospital waiting time, patient discomfort and also radiation exposure [3,4].

## Materials and Methods

### Study population

This prospective study was performed on n=93 patients with age range 30-55 years (mean age 51 ± yrs) referred for myocardial perfusion SPECT. The study population (n=93) was divided into 02 major groups on the basis of disease status (either known or without known CAD). Group-I included (n=29) 31% patients with known coronary artery disease, out of which (n=13) 45% patients were those with reported inferior wall MI were placed in group-I-a, while (n=16)

55% patients with reported RCA territory lesion on coronary angiography were placed in group-I-b respectively. Group-II included n=64 (69%) patients without known coronary artery disease. The patients in group-II further categorized on the basis of perfusion defects seen on supine imaging on MPS involving either inferior wall or in anterior/anteroseptal wall, out of which (n=40) 62% of patients were those with inferior wall defect were placed in group II-a while (n=24) 38% were those with anterior or anteroseptal wall defects were placed in group II-b. Group-II-a patients were subcategorized as obese (BMI ≥ 30, n=17) and non-obese (BMI ≤ 30, n=23) in II-a-i and II-a-ii respectively [5]. While group-II-b patients were subcategorized as male (due to attenuation by thick chest wall; n=10) and female (due to breast tissue attenuation; n=14) in subgroups II-b-i and II-b-ii respectively as shown in the Table 1.

Groups	No. of patients (n=93)
<b>Patients with known CAD (n=29)</b>	
IWMI lesion (documented either on trop/ecg/echo) (Non-invasive)	13 (14%)
Pts. with RCA lesion (Invasive)	16 (17%)
<b>Patients without known CAD (n=64)</b>	
• Pt with inferior wall defect on supine MPS (n=40)	
a) Obese (BMI>30)	17 (18%)
b) Non obese (BMI<30 )	23 (25%)
• Pt with anterior wall defect on supine MPS (n=24)	
a) Male (atten. due to thick chest wall)	10 (11%)
b) Female (atten. due to breast tissue )	14 (15%)
Total	93 (100%)

**Table 1.** Showing distribution of study population.

The rest imaging was obviated in case of complete improvement of the defect in the prone position and was included when defect persisted on prone acquisition.

### Exercise myocardial perfusion protocol

Patients performed a treadmill exercise test using a standard Bruce protocol. Leads aVF, V1, and V5 were continuously monitored and a 12-lead Electrocardiogram (ECG) was recorded with the exercise. At peak exercise, a weight-adjusted dose of 99 mTc-sestamibi/99 mTc-tetrofosmin (296–370 MBq 8-10 mCi) was injected, and exercise was continued for 1 min after injection. MPS acquisition was initiated 20-30 minutes after isotope injection. Whenever possible, β-blockers and calcium channel blockers were discontinued 24 hours before testing, and nitrates were discontinued at least 6 hours before testing [6].

### Pharmacological stress myocardial perfusion protocol

Patients were instructed not to consume caffeine containing products for 24 hours before the test. Adenosine was infused intravenously at a rate of 140 ug/kg/min for 6 min. At the end of the third minute of infusion, weight adjusted 99 mTc-sestamibi/99 mTc-tetrofosmin was injected. Similarly persantine

(Dipyridamole) was infused at 0.56 mg/kg (142 ug/kg/min) intravenously over a 4 minutes period. After the infusion was finished, radiopharmaceutical was injected intravenously 3-5 min post infusion. Then image acquisition was initiated approximately 30 min after isotope injection [7].

### MPS acquisition protocol

All patients underwent one day stress (supine-prone) and rest MPS protocol with acquisition protocol of a non-circular, counter clockwise with starting angle of 1350, head in position, and 32 projections at 25 seconds per projection for Tc-99 m in the supine position. For prone acquisition protocol, we used non-circular, counter clockwise with starting angle of 2250, feet in position, and 32 projections at 25 seconds per projection. Tc-99 m sestamibi (weight-adjusted dose of 8-10 mCi) was then injected during stress, and supine 16-frame with occasional gated MPS (100% acceptance window) was initiated 30 minutes after exercise or pharmacological stress, followed by the prone acquisition. Two gamma cameras were used in our study for imaging of patients, dual head Phillips cardio MD and Dual head Siemens' Signature series. Filtered back projection applying butterworth filter, short-axis, vertical long axis, and horizontal long-axis tomograms were generated for both the supine and prone data sets with automatic reorientation using Jetstream (for CardioMD camera) and Syngo MI software (for signature seimen camera)

resulting reconstructed image as 17 segment standard model [8].

### Image interpretation

The supine defects were accordingly as persisting or disappearing in the prone position. The persisting defects in the prone underwent rest imaging [9,10]. The perfusion defect improvement with positional change had to be complete to be considered as disappearing in the prone. New apparent anterior or antero-septal defects in the prone position were attributed to sternal or rib attenuation artifact and did not alter the classification. Semiquantitative visual interpretation of SPECT perfusion images used short-axis and vertical long-axis tomograms divided into 17 segments for each patient. Each segment was scored by consensus by 2 expert observers using a 5-point scoring system (0=normal; 1=equivocal; 2=moderate reduction of radioisotope uptake; 3=severe reduction of radioisotope uptake; and 4=absence of detectable radiotracer in a segment).

To further define the results as normal or abnormal, the Summed Stress Score (SSS) was calculated by adding the scores of the 17 segments of the stress Tc-99 m tetrofosmin/sestamibi images. SSS <4 were considered normal, 4 to 8 mildly abnormal and >8-13 moderate abnormal >13 severely abnormal. The SSS had to be <4 and the final scan interpretation had to be normal or probably normal, as any other case was considered abnormal. Moreover, the difference in SSS (SSS in supine image minus SSS in prone image) was calculated for each patient. Then the mean value of SSS difference for each defect group (disappearing or remaining defect group) was calculated. When rest imaging was done, segments were scored as well. Results were compared with clinical data and coronary angiography findings [11].

### Statistical analysis

The Summed Stress Scores (SSS) were calculated by using one sample t test on IBM SPSS Statistics Software version 20 to compare the means of supine SSS versus prone SSS.

## Results

A total of 93 patients were assessed of which 72 (77.4%) were males while 21 (22.6%) were females. The mean age of patients was  $56.93 \pm 9.41$  years. The mean BMI of the patients was  $28.34 \pm 4.41$ . Out of 93 patients, 50 (63.4%) had history of co-morbid hypertension including 38 (40.9%) having also diabetes mellitus, 16 (17.2%) were smokers, 7 (8.1%) had family history of coronary artery disease, while 5 (5.8%) had dyslipidaemia. 15 patients had no history of co-morbid conditions. Using the WHO's Asian BMI cut-offs for high risk of cardiovascular disease, 51 (59.4%) of the patients were Obese having BMI  $\geq 30$ .

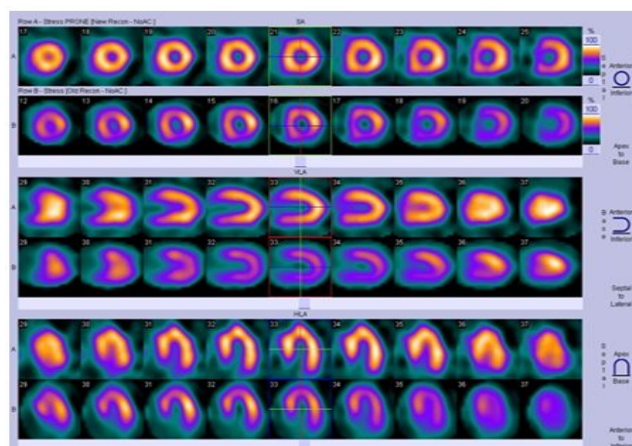
Myocardial perfusion SPECT was performed in 93 patients in whom the standard supine acquisition study was concluded to be revealing equivocal/abnormal findings (inferior or anterior wall defect) in all the patients. Rest MPS was excluded in patients with normal prone study,  $n=54$  (60.2%) while it was conducted in remaining patients whose prone study remained abnormal,  $n=39$  (39.8%) [12].

In group-I-a, patients ( $n=13$ ) with documented inferior wall MI in whom supine images of MPS revealed perfusion defects in the

inferior wall, 31% (4/13) were interpreted as normal on prone images, hence rest part of MPS was excluded. On echocardiography, there was normal wall motion in the inferior wall. While on follow up these patients presented with persisting symptoms and were advised for coronary angiography, which showed patent RCA. Among this subgroup, remaining 69% (9/13) were interpreted as abnormal with persisting defect on prone, hence rest was done, which showed complete reversibility in 54% (7/13) and fixed defects in 15% (2/13) patients [13]. On echocardiography there was hypokinesia of the inferior and lateral wall in those with complete reversibility 54% (7/13), and akinetic inferior wall in those with fixed defects 15% (2/13) on rest. When followed up all these 69% (9/13) patients had recurrent symptoms of dyspnoea and mild to moderate chest pain, and were advised for coronary angiography which proved to be normal in 8% (1/13) patient with fixed perfusion defects, and moderate to severe lesion in the RCA territory in remaining 61% (8/13) patients [14].

In group-I-b ( $n=16$ ), among patients with reported RCA lesion on angiography, supine images showed abnormal perfusion defects in the inferior wall in all these patients,  $n=16$  (100%). When done on prone, 13% (2/16) were interpreted as equivocal defect in the inferior wall, which on rest showed complete reversibility. Remaining 87% (14/16) were shown to have abnormal perfusion defect on prone in the corresponding territory, which on rest showed complete reversibility in 37% (6/16) patients. While 63% (10/16) were with fixed defect. On echocardiography, 37% (6/16) had dyskinetic and 63% (10/16) had hypokinetic inferior wall. When followed up all the patients had recurrent symptoms of dyspnoea and mild chest pain, and 44% (7/16) were on conservative treatment, while 56% (9/16) were advised for PCI. Therefore among group-I patients, true positive cases were 76% (22/29), true negative were 14% (4/29), false negative were 7% (2/29) and false positive was only 3% (1/29) as mentioned in the following [15]. Hence sensitivity and specificity of prone MPS among group-I patients of known coronary artery disease came out to be 91.6% and 80% respectively and positive and negative predictive values of 95.7% and 66.7% respectively with diagnostic accuracy of 90%.

In group-II-a-i (Obese,  $n=17$ ) and II-a-ii (Non obese,  $n=23$ ), supine MPS revealed inferior wall defect in all these patients 100% (40/40). In group-II-a-i ( $n=17$ ), when on prone, 77% (13/17) patients were interpreted as normal as shown in Figure 1.



**Figure 1.** 45 years old male with no history of CAD, shows significant improvement on prone.

Hence no rest was done in these patients. When followed up clinically, 41% (7/17) of these normal prone interpreted patients had persisted symptoms and were advised for echocardiography, which showed hypokinetic apex and inferior wall and then on angiography revealed patent RCA. While remaining 35% (6/17) patients were symptomless and no soft/hard event occurred. While remaining 23% (4/17) patients were interpreted as abnormal perfusion defect in inferior wall on prone, which on rest showed complete reversibility. When followed they had hypokinetic inferior wall on echocardiography, and were labeled with significant RCA lesion on angiography [16].

Among subgroup-II-a-ii non-obese patients (n=23), 74% (17/23) patients were interpreted as normal on prone. Hence no rest was done in these patients. On clinical follow up, 35% (8/23) of these patients had persisted symptoms and were advised for echocardiography, which showed hypokinetic inferior wall and then on angiography 9% (2/23) of these patients revealed moderate to severe lesion in the RCA and LAD while remaining 26% (6/23) were normal on angiography. Remaining 39% (9/23) of these patients were symptomless and no any further investigation advised [17].

Remaining 26% (6/23) patients of this subgroup were interpreted as abnormal on prone, which on rest showed reversible perfusion defect in 9% (2/23) and fixed defect in 17% (4/23) patients. On follow up, all 26% (6/23) patients had persisted symptoms and when performed angiography, were revealed moderate to severe stenosis in LAD and RCA. In subgroup-II-b-I among 10 male patients, 60% (6/10) presented with anterior wall defect and 40% (4/10) with antero-septal defect on supine MPS [18]. On prone, all 60% (6/10) with anterior wall defect and 20% (2/10) with antero-septal defect were improved as normal, hence no rest was done. These were also normal on echocardiography. And on follow up, all patients were symptomless and no soft/hard event occurred. While remaining 20% (2/10) patients with antero-septal defect showed persisting antero-septal defect on prone, which were reversible on rest. On echocardiography they had dyskinetic inferior wall. When followed up, they had recurrent symptoms of dyspnoea and mild chest pain, and were advised for angiography which showed lesion in RCA (Figure 2) [19].

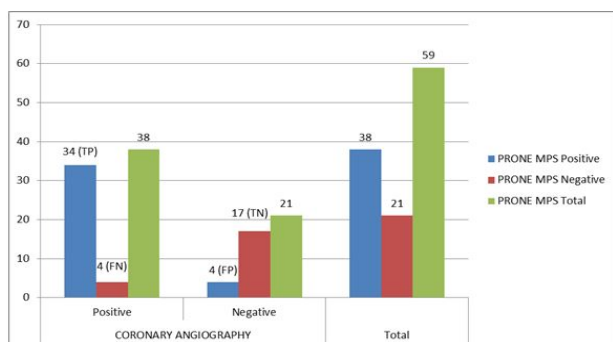


Figure 2. Coronary angiography.

In subgroup-II-b-ii among 14 female patients, 71% (10/14) presented with anterior wall defect while 29% (4/14) with antero-septal defect on supine, 86% (12/14) were improved as normal on prone interpretation. Hence rest was obviated in. These were also normal on echocardiography. And on follow up, all patients were symptomless and no soft/hard event occurred. Remaining 21% (3/14) underwent rest, which showed reversible defect. And on follow up these patients were advised angiography which showed patent RCA as shown in Table 1.

When comparison was made to observe the concordance between findings of prone MPS and angiography among group-II patients with unknown coronary artery disease, angiography was found to have done of only 47% (30/64) patients on clinical follow up. Therefore among group-II patients, true positive cases were 40% (12/30), true negative were 43% (13/30), false negative were 7% (2/30) and false positive were 10% (3/30) as mentioned in the following. Hence sensitivity and specificity of prone MPS among Group-II patients came out to be 86% and 81.3% respectively and positive and negative predictive values of 80% and 87% respectively with diagnostic accuracy of 83%.

Hence sensitivity and specificity of prone MPS among all patients who also underwent angiography n=59 (63.4%) out of 93, taking angiography as "gold standard", came out to be 89.5% and 81% respectively and positive and negative predictive values of 89.5% and 81% respectively with diagnostic accuracy of 86%. *Chi-Square* (pearson) test was applied collectively on both group-I and II for statistical analysis which revealed p value of "0.005".

## Discussion

This study was conducted on the theme that prone MPS imaging reduces artifact either of inferior and anterior wall associated with supine MPI study. The mean age group of study population was  $56.93 \pm 9.41$  years while Islam S, et al. showed mean age  $60 \pm 5$  years. The reason for younger age limit in our population may due to fact that most of our patients had some co-morbids or sedentary life style [20].

It is also found from the study that males were more prone to coronary artery diseases which are matched from previous study reported by Samad et al. for male preponderance. Literature review also revealed that young female patients have lower mean value for coronary artery disease due to estrogen protective effects.

Besides that it was also concluded from the study that hypertension and diabetes were two most important cardiovascular risk factors which were more prone our patients to cardiovascular disease. Our results were correlated with previous study done by Chiha et al. who concluded that approximately 44% of the reduction in acute coronary syndromes was secondary to a decline in these two/three most important cardiovascular risk factors.

In this study, patients with supine MPS demonstrating findings that would have rendered the interpretation of the inferior and anterior wall as equivocal or abnormal underwent prone imaging. The present study confirms that prone imaging reduces artifact inferior wall abnormalities associated with supine study, leading to more appropriate clinical decisions and shortening the hospital waiting period and patient discomfort. Most importantly, rest myocardial perfusion study can be safely excluded in patients with an inferior wall "disappearing" defect by prone SPECT. This provides an excellent approach to limit radiation exposure by avoiding additional radiotracer infusion. Soft tissue attenuation artifacts constitute a major shortcoming of myocardial perfusion imaging. Various techniques to improve specificity have been evaluated, but to date there has been no clear definition of which is the best one. It is generally accepted that attenuation artifacts are less frequent with Tc 99 m tracers than with Thallium-201 (TI-201) as they are very little redistribution in case of sestamibi or tetrofosmin.

A common problem with MPS is the artifactual reduction in apparent radiotracer uptake due to soft-tissue attenuation, resulting in reduced accuracy of interpretation. Most commonly, photon attenuation results in reduced specificity for detecting CAD; however, attenuation can also affect sensitivity by increasing the range of normal limits. Various methods have been investigated to solve this problem. It is suggested that inspecting only planar projection images can help in identifying photon attenuation in the inferior wall due to the left hemidiaphragm or in the anterior wall in females with large breasts. However, relying exclusively on planar images for this purpose is likely to reduce sensitivity for the detection of true abnormalities. So we need some better method/tool to identify all these artifacts for which we use prone imaging as tool. The prone position has been shown to reduce diaphragmatic attenuation and patient motion on MPS. The reduced attenuation is considered to be due to a downward displacement of the diaphragm relative to the myocardium in the prone position, and the reduced patient motion is considered to be due to the close contact of the anterior portion of the chest to the imaging table. In our study results 23 patients who showed abnormal supine MPS were due to diaphragmatic attenuation which resulted in normal perfusion images on prone MPS. 12 were those who are abnormal supine MPS was due to motion artefact which resulted in normal prone images. The prone acquisition, however, has also been reported to produce artifactual anteroseptal defects, thought to be due to the closer position of the heart to the bony structures of the anterior chest wall. It is previously documented that in patients who have inferior wall perfusion defects on supine images and have normal prone images, the prognosis is excellent and equal to that observed in a cohort of patients with normal MPS using supine imaging alone. We have performed combined supine and prone imaging in 93 patients and have found that approximately 95% of patients are able to tolerate the prone position for the period required for adequate count statistics.

Prone imaging yields more accurate scintigraphic interpretations without any additional cost, it is inexpensive and it does not deliver any extra radiation to the patient. It is associated with increased inferior and septal wall counts, less patient motion, patient discomfort and cardiac drift. However, it is less suitable for females with large breasts and obese patients but if applied showed drastic results. Direct attenuation correction systems are commercially available. Although these systems tend to decrease the rate of equivocal interpretations to a greater extent than prone imaging, they require high cost hardware and software products.

The use of combined supine and prone quantitative imaging in overcoming diaphragmatic and/or breast attenuation artifacts has been evaluated before. Data from several researchers have shown significantly increased specificity without compromising sensitivity for the diagnosis of CAD. This is in agreement with the results of our study, where a sensitivity of 89.5% and a specificity of 81% were shown. Katayama, et al. have similarly demonstrated that prone stress TI-201 study tends to improve the specificity of detecting coronary disease in the inferior wall. On the other hand, they showed that sensitivity is reduced when compared to stress-rest supine images.

In our study population, rest acquisition was also performed in patients with defects on supine SPECT that did not disappear on prone imaging. There is seen an excellent usefulness of combined supine and prone acquisitions on attenuation artifacts in our study. Segall and Davis have demonstrated that specificity for RCA was dramatically better (90% vs. 66%) when patients were submitted to prone image acquisition compared to supine. Furthermore, the overall effect on the detection of CAD was an improved accuracy and higher specificity (82% vs. 59%) without significant loss of sensitivity (75% vs. 79%). In addition, Hayer et al. concluded that patients with inferior wall defect in the supine position that was not present in the prone image had similar low risk of cardiac events, when compared with those that had normal supine only studies.

False negative and false positive results of prone imaging were seen in (4/59=6.8%) each of our study population. The development of coronary collateral circulation could be a possible explanation for the false negative results. Thus, positional change may not always be sufficient to differentiate attenuation artifacts from CAD. Although some authors believe that prone imaging is associated with increased camera to chest wall distance and lower total myocardial counts when compared to supine position, in this work prone image quality was very satisfactory. This is in agreement with a recent study by Gutstein et al. which showed that prone and supine imaging is associated with comparable good image quality in the non-obese population, even though half-time acquisition has been used.

Anterior wall defects are most common in women. Although some believe that positional change mainly contributes to the disappearance rate of diaphragmatic attenuation, it is a confirmed knowledge that combined supine and prone limited to

24 patients only including both male and female with anterior and antero-septal defect, 83% of the anterior and antero-septal wall defects disappeared in the prone image and subsequently, the rest perfusion study was properly obviated. Anterior wall defects in the supine acquisition that were absent with positional change tended to represent breast attenuation artifacts.

## Conclusion

The addition of prone position to stress supine myocardial scintigraphy overcomes soft tissue attenuation hence decreases the false positive rates and leads to more accurate results. Furthermore, it increases specificity without compromising sensitivity for the diagnosis of CAD. It has a key benefit of preventing unnecessary further investigations and treatment, and also indicating a better prognosis. This would save time, money and enhance the diagnostic accuracy, while at the same time saving patients from the risk involved in unnecessary tests, whilst minimizing radiation exposure. Moreover, it could possibly be a useful and practical method of obviating unnecessary referrals to coronary angiograms, especially in low-risk patients.

In our study, the addition of prone acquisition to traditional supine MPS SPECT has been proven to be an easy and efficient way to reduce attenuation artifacts involving inferior, anterior and antero-septal wall especially in patients without already known coronary artery disease, leads to a significant improvement in the specificity of this imaging technique. Since decisions for catheterization after MPS are frequently based on risk assessment, our findings suggest that the addition of the prone acquisition to supine MPS might lead to more appropriate clinical decisions.

## Limitations

Several limitations of the supine and prone MPS technique should be mentioned. Duration of the entire study is only 6 months; hence the duration of the clinical follow up was also limited to the 3 months only. The combined imaging requires additional camera time that may not be available in many hospitals. Additionally, a small proportion of patients cannot lie in the prone position for the time required for MPS. Regarding our study design, because the supine images were interpreted before the prone images, the supine results influenced the combined supine and prone interpretation. However, it was not our intent to demonstrate that prone imaging is superior to supine but, rather, that the combined approach is more effective than supine imaging alone. In addition, gated SPECT could not be performed due to technical issues which will improve the confidence level of interpretation. Here, we only present the preliminary results of an ongoing study and further trials are still required on this issue.

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