

# Comparative accuracy of supine-only and combined supine-prone myocardial perfusion imaging in men

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**Background.** Combined supine-prone myocardial perfusion imaging (CSP MPI) has been shown to reduce attenuation artifact in comparison to supine-only (SU) MPI in mixed-gender populations with varying risk for coronary artery disease (CAD), often where patients served as their own controls. However, there is limited direct comparison of these imaging strategies in men.

**Methods.** 934 male patients underwent CSP or SU MPI. Diagnostic certainty of interpretation was compared. Within the cohort, 116 were referred for left heart catheterization (LHC) to assess for CAD. Sensitivity, specificity, and area under the curve (AUC) were compared with additional analysis based on body mass index (BMI).

**Results.** 597 patients completed the SU protocol and 337 patients completed the CSP protocol. Equivocal studies were seen more frequently in the SU group (13%) than in the CSP group (4%,  $P < .001$ ). At catheterization, the specificity for CSP MPI of 70% was higher than 40% for SU MPI ( $P = .032$ ). The CSP AUC ( $0.80 \pm 0.06$ ) was significantly larger than SU AUC ( $0.57 \pm 0.05$ ,  $P = .004$ ). CSP specificity was significantly higher in obese patients.

**Conclusions.** CSP MPI increases diagnostic certainty and improves test accuracy for CAD detection in men with CAD risk factors, especially obese patients, compared to SU MPI. (J Nucl Cardiol 2016;23:1470–6.)

**Key Words:** Myocardial perfusion imaging • image artifacts • tetrofosmin • coronary artery disease

## Abbreviations

AC	Attenuation correction	LHC	Left heart catheterization
BMI	Body mass index	MPI	Myocardial perfusion imaging
CABG	Coronary artery bypass grafting	PCI	Percutaneous coronary intervention
CAD	Coronary artery disease	SPECT	Single photon emission computed tomography
CSP	Combined supine-prone	SU	Supine
EKG	Electrocardiogram		
FFR	Fractional flow reserve		

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## INTRODUCTION

Although stress single photon emission computed tomography (SPECT) MPI is the predominant noninvasive screening modality for the detection of obstructive coronary artery disease (CAD), artifacts often confound accurate image interpretation.<sup>1</sup> One approach that has been reported to enhance the diagnostic accuracy of MPI is the use of combined supine-prone MPI (CSP MPI) instead of supine-only MPI (SU MPI). The benefit of prone imaging has been attributed to a reduction in photon attenuation resulting from a variety of factors. These include downward displacement of the diaphragm and sub-phrenic organs, compression of the soft tissue of the anterior thorax including breast, anterior shifting of the heart, and reduction of patient motion.<sup>2–5</sup> In studies using patients as their own controls, the incremental diagnostic accuracy of adding prone to supine MPI has been reported in combined populations of women and men, including obese patients and exclusively female cohorts.<sup>6–8</sup> However, there is limited data directly comparing these two imaging strategies, particularly in exclusively male cohorts.<sup>4,7</sup> In addition, there may be gender-specific differences in the type of artifact that is reduced, and the degree to which interpretative accuracy is affected.<sup>5,8</sup>

Despite its potential in improving diagnostic accuracy, CSP MPI is not widely utilized. We conducted a comparative assessment of the diagnostic accuracy of CSP MPI vs SU MPI in men in our nuclear laboratory. The aim of this study was to retrospectively compare the diagnostic certainty of interpretation, extent of attenuation artifact, and accuracy of CAD detection in men undergoing either CSP MPI and SU MPI with regadenoson.

## METHODS

### Patient Population

In this retrospective cohort study, we identified all patients who underwent rest and regadenoson stress 99-m technetium tetrofosmin MPI at the Veterans Administration Medical Center in Lake City, FL from January 2012 to July 2013. During this time, the laboratory routinely alternated between CSP MPI and SU MPI. Of 973 consecutive patients who underwent MPI, 39 were female and were excluded from further analysis. Of the remaining 934 male patients, 424 were protocolled for CSP MPI. Of these, 87 patients (20%) of these patients did not undergo prone imaging, but did complete SU MPI. Therefore, 597 SU MPI and 337 CSP MPI patients were studied. Of these 934 patients, 116 patients underwent left heart catheterization (LHC) within 6 months,

either due to an abnormal stress MPI or persistent cardiac symptoms after a normal MPI.

## Clinical Assessment

The decision to perform a regadenoson MPI was made by primary care and cardiology providers. For primary care providers, a standardized computer ordering algorithm helped direct appropriate stress test selection based on the patient's age, gender, typical vs atypical symptoms, number of cardiac risk factors, CAD history, physical limitations, and baseline EKG findings. Cardiology providers were not required to use this screening tool, although individualized screening for appropriateness of consultation requests was routine. In addition, an experienced nuclear medicine physician routinely screened MPI requests to confirm clinical appropriateness, generally based on their interpretation of existing appropriate use criteria.<sup>9</sup> Previous review of the above screening methods suggests a 10% inappropriate test rate in our laboratory.<sup>10</sup>

On the day of stress testing, the performing physician or a trainee obtained a cardiac-focused clinical history including medical history, a review of cardiovascular risk factors and symptom complaints. Demographic data and cardiovascular risk factors were identified by chart review from the electronic medical record.

## Stress Protocol

The only form of nuclear stress testing performed at the Lake City VA was regadenoson MPI. Patients selected for treadmill MPI had their studies performed at another VA site and were not included in this study. Regadenoson was administered as recommended by the manufacturer with appropriate monitoring.

## Image Acquisition and Reconstruction

Rest and stress MPI were performed using 99m Tc tetrofosmin, 8–10 mCi at rest and 40 mCi in the stress study (up to 50 mCi for morbidly obese patients with BMI  $\geq$  40 kg/m<sup>2</sup>). This stress dosing was selected because lower dosing had resulted in count-poor images, likely due to a large proportion of obese and morbidly obese patients in our population.

A Philips Vertex dual-head SPECT camera and a low energy, high-resolution collimator were used. Step and shoot acquisition was performed. 180° acquisition, 64 steps, 20 s per step in the stress supine images. In CSP, images in the prone position were acquired after pharmacologic stress and were 15 s/step. Rest studies were performed in the supine position only and were 25 s/step. In the morbidly obese patients, the time per step was 30 s. Filtered back projection and filter with a cut-off frequency of 0.50, order 5.0, were used. The pixel size was 6 to 8 mm. Reconstruction and images display were performed in a JETStream Workspace Cardiology Module version 3.0. Quantitative analysis of the supine studies was performed using AutoQuant version 6.5. For CSP studies, only qualitative, not quantitative, analysis of perfusion defects was performed. Attenuation correction, scatter compensation, and resolution recovery were not applied.

## Image Interpretation

Experienced readers certified in Nuclear Medicine interpreted the MPI. Interpretation was based on the American Society of Nuclear Cardiology Guidelines for Reporting.<sup>11,12</sup> Visual analysis was the main method of interpretation with adjunctive use of software quantitation algorithms (available only for supine images). Segmental analysis was based on the 17 segment model. The severity of the perfusion abnormality was assessed visually using the 5-point scale.

## Diagnostic Certainty

As part of a diagnostic certainty assessment, MPIs were classified as definite or equivocal. Definitive studies were reported as normal or abnormal for the presence of infarct or ischemia. Equivocal studies were reported as “probably normal” or “probably abnormal”, and reports often contained commentary on the source of diagnostic uncertainty.

## Artifact Size Assessment

In an early subset of the 271 patient within the CSP group (81%) who had their studies performed from January 2012 through February 2013, artifact size in the supine and prone positions was compared. We collectively refer to “inferior artifacts” (in the inferior, inferolateral, and inferoseptal walls) as those attributable to diaphragmatic and soft tissue attenuation, gastrointestinal trace interference, motion artifact, and ramp filter artifact. The sizes of these artifacts were scored by an experienced reader using a semi-quantitative scoring system. A score of 1 corresponded to no or minimal artifact. A score of 2 corresponded to small artifact (involving up to two segments). A score of 3 corresponded to medium-sized artifact (involving three or four segments), and a score of 4 corresponded to a large artifact (involving five or more segments). To specifically assess for prone-induced artifacts, we separately identified the appearance of prone-specific “anterior artifacts” (in the anterior, anterolateral, and anteroseptal walls), not seen on supine datasets.

## Coronary Angiography

Left heart catheterization (LHC) with coronary angiography performed within a 6-month time frame was reviewed by a group of cardiologists, radiologist, and nuclear medicine physician for correlation with MPI. Luminal stenosis was 191 visually assessed by experienced cardiologists. Greater than 50% left main or >50–70% luminal stenosis of other coronaries (with supporting fractional flow reserve data when appropriate) was considered significant for the presence of obstructive CAD. If the physiologic significance of a 50% or greater lesion was uncertain, fractional flow reserve (FFR) was performed. An FFR value less than 0.75 was considered significant. In order for a correlation to count as a true positive, a region of ischemia had to correspond to at least one abnormal coronary territory.

## Statistical Analysis

Continuous variables were expressed as mean  $\pm$  standard deviation (SD), and categorical variables were expressed as

percentages (%). Paired *t* tests were used to compare differences in paired continuous data. Fisher’s exact test or Chi-squared tests were used to compare differences in categorical data between groups. For the image quality sub-study, Wilcoxon signed rank tests were used to compare differences in paired discrete data. To assess the diagnostic accuracy of SU and CSP, receiver-operating-characteristic (ROC) curve analyses were performed. The area under the curve (AUC) was compared using the method of DeLong, and a standard error was calculated.<sup>13</sup> All statistical tests were 2-tailed and *P* < .05 was significant. This study was approved by our Institutional Review Board.

## RESULTS

### Demographics

597 MPI patients completed the SU protocol and 337 patients completed the CSP MPI protocol. In the overall group, the mean age was  $65 \pm 10$  years. Over half of the patients (*N* = 519, 55%) were obese with a BMI  $\geq 30$  kg/m<sup>2</sup>, of which 93 (10%) patients were morbidly obese (BMI  $\geq 40$  kg/m<sup>2</sup>). Hypertension, hyperlipidemia, diabetes mellitus, family history of early CAD, and current tobacco use were the cardiovascular risk factors assessed for in this population. Two or more risk factors for CAD were present in 833 (89%) patients. In addition, 18% of patients had a history of myocardial infarction or coronary revascularization (CABG and/or PCI). There was no significant difference in the age, number of cardiovascular RF’s, presence of obesity, and past history of CAD between the SU and CSP MPI groups. Demographics are summarized in Table 1.

### Diagnostic Certainty

Diagnostic certainty was evaluated in 597 SU studies and 337 complete CSP studies, of which 94 (10%) were equivocal. Equivocal studies were seen more frequently in the SU group (79, 13%) than in the CSP group (15, 4%, *P* < .001). In most equivocal studies, diaphragmatic attenuation was seen. Motion artifact, brightness scaling artifact, ramp filter artifact, and overlap artifact were also identified.

### Artifact Size

A large subset of CSP studies (*N* = 271) were evaluated for artifact size involving the inferior, inferoseptal, and inferolateral walls in the prone and supine positions. These artifacts were predominantly due to soft tissue attenuation. Large or medium artifact was seen in 33% (*N* = 95) in the supine position vs 8% (*N* = 22) the prone position (*P* < .0001). Table 2 shows the

**Table 1.** Patient demographics based on stress protocol completed

Variable	Total (N = 934)	SU (N = 597)	CSP (N = 337)	P value*
Age (years)	65 ± 10	66 ± 10	65 ± 9	.28
Number of RF				
0-1	101 (11%)	56 (11%)	45 (13%)	.13
2-5	819 (89%)	445 (91%)	374 (87%)	.87
BMI				
<30 kg/m <sup>2</sup>	419 (45%)	222 (45%)	197 (46%)	.90
≥30 kg/m <sup>2</sup>	499 (55%)	267 (55%)	232 (54%)	
CAD history	168 (18%)	106 (18%)	62 (18%)	1.0

For all fields, mean ± standard deviation or number (%) is shown

SU, supine-only myocardial perfusion imaging; CSP, combined supine-prone myocardial perfusion imaging; RF, risk factors for coronary artery disease; BMI, body mass index; CAD, coronary artery disease

\*No significant differences were noted between the SU and CSP groups in the listed parameters, with  $P < .05$  denoting significance

comparison of inferior artifact size in the prone and supine positions. Within the CSP group, 149 patients (55%) were obese (BMI ≥ 30 kg/m<sup>2</sup>) and 122 (45%) were non-obese (BMI < 30 kg/m<sup>2</sup>). In the obese and non-obese subgroups, inferior artifact size generally decreased with prone imaging. The average change in artifact size from supine to prone in the obese subgroup was 0.7 ± 0.8 and in the non-obese patients was 0.8 ± 0.7, which was statistically insignificant ( $P = .26$ ).

The appearance of prone-specific artifacts in the anterior, anteroseptal, and anterolateral walls was also assessed in the CSP studies. With prone position, new anterior wall artifacts were seen in 43 patients (15%) and a new anteroseptal wall artifact was seen in only 1 patient. These artifacts were all small in size, mild in severity, and easy to recognize, making them unlikely to affect the final interpretation.

### Left Heart Catheterization

The overall catheterization rate was 12%. Of the 116 patients who underwent LHC, 15 (13%) underwent FFR. Similar rates of LHC were seen between groups. Catheterization was performed in 13% of the SU group (N = 77) and 12% (N = 39) of the CSP group. Of the patients who underwent LHC, 74% (n = 86) had an abnormal MPI while 26% (N = 30) had a normal MPI with persistent symptoms.

Flow-limiting CAD was detected in 67 of 116 patients (58%). One-vessel CAD was seen in 25 patients (22%). Multi-vessel CAD was seen in 42 patients (36%). There were no significant differences in the presence or absence of significant CAD in the SU (46%) and CSP groups (50%,  $P = .71$ ). In 43 (37%) patients, LHC did

not confirm MPI impression. SU MPI was performed in the majority of these non-confirmatory LHC cases (65%). One study was excluded due to poor technical quality, and another due to an equivocal interpretation.

Figure 1 demonstrates the ROC curves for the CSP and SU MPI patients who underwent LHC. The CSP AUC of 0.80 ± 0.06 was significantly larger than SU AUC (0.57 ± 0.05,  $P = .004$ ). While the CSP AUC was significantly different from the null hypothesis ( $P < .001$ ), the SU AUC was not ( $P = .20$ ). Although sensitivity in the CSP MPI group (89%) was higher than in the SU MPI group (74%, 95% CI), the difference was not statistically significant ( $P = .167$ ). The specificity for CSP MPI of 70% was, however, significantly higher than 40% for SU MPI ( $P = .032$ ). In particular, the false positive rate attributable to inferior wall artifacts was high in SU MPI patients (64%) vs CSP MPI patients (27%,  $P < .001$ ).

In the LHC group, 72 patients (62%) were obese with a BMI ≥ 30 kg/m<sup>2</sup>. Test characteristics are summarized in Table 3. In the obese subgroup, sensitivity was greater than 85% for either positioning protocol. However, false positive rates were 40% higher for SU MPI vs CSP MPI in obese patients, compared to 20% higher in patients with BMI < 30 kg/m<sup>2</sup>, and this approached statistical significance ( $P = .06$ ). The high false positive rate in the obese subgroup was driven by major differences in MPI specificity—the specificity for CSP MPI was 64% compared to only 26% in the SU MPI group ( $P = .034$ ). Similarly, for obese patients, the area under the curve was significantly higher in the CSP groups (0.79 ± 0.08) than in the SU group (0.57 ± 0.06,  $P = .030$ ). In 42 non-obese patients, the specificity for CSP MPI in non-obese patients was 55% vs 22% in the CSP and SU MPI groups, respectively, but this did not

**Table 2.** Comparison of “inferior” artifact size in CSP subgroup

Artifact size	CSP-Prone (N = 271)	CSP-Supine (N = 271)	P value*
None <sup>1</sup>	158 (58%)	31 (11%)	<i>P</i> < .001 *
Small <sup>2</sup>	92 (34%)	145 (54%)	
Medium <sup>3</sup>	20 (7%)	82 (30%)	
Large <sup>4</sup>	1 (<1%)	13 (5%)	

*CSP-Prone*, combined supine-prone myocardial perfusion images in the prone position; *CSP-Supine*, inferior, inferolateral, and inferoseptal artifacts collectively referred to as “inferior” artifacts were graded based on size on a scale from 1 through 4 in a large subset of CSP patients (1 = none, minimal, 2 = small, 3 = medium, and 4 = large)

\**P* < .05 is considered significant for Wilcoxon signed rank test comparing the total distribution of “inferior” artifact sizes in CSP-Prone and CSP-Supine subgroups

achieve statistical significance in this small subgroup (*P* = .14). The sensitivity was higher in the SU group (100%) than in the CSP group (75%, *P* = .02), but it is notable that the sample size was small.

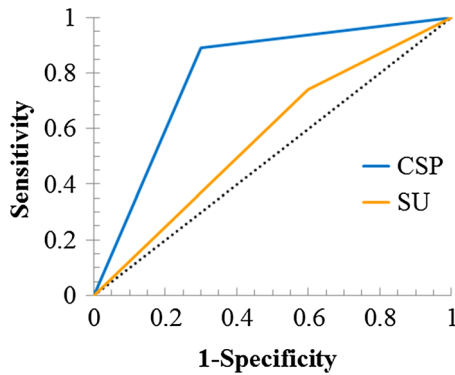
### DISCUSSION

In this comparative study of CSP MPI and SU MPI in men with CAD risk factors, the use of CSP imaging improved diagnostic certainty during interpretation and accuracy for CAD detection. In the artifact sub-study, one-quarter of the patients demonstrated resolution of large or medium size attenuation artifacts observed in the supine position with the addition of prone imaging. This was largely attributable to less diaphragmatic and soft tissue attenuation, and was observed in obese and non-obese patients. Among those who underwent LHC, diagnostic accuracy for CAD detection was much greater with CSP MPI than SU MPI. This was achieved mainly through an improvement in specificity, with no compromise in sensitivity. The diagnostic benefit was most apparent in obese patients because of the high false positive rate with SU-only imaging in this subgroup.

Increased specificity for CAD detection is a known benefit of CSP MPI. The observed specificity rate of 70% is the middle of previously reported rates ranging from 55% to 92%.<sup>6,14-17</sup> It is possible that post-test referral bias may have lowered specificity in this study overall.<sup>18,19</sup> Nonetheless, the important finding here is the difference in diagnostic accuracies between CSP and SU MPI patients. Previous protocols have demonstrated differences using patients as their own controls. This study, in contrast, directly compared groups of patients who completed protocol. Unlike other direct comparison studies in which patients are selected for CSP MPI on the basis of some criteria (i.e., obesity or the presence of artifact), patients were protocolled for either type of study independent of such criteria.

This study has some additional unique features. Previous studies included low-risk patients and mixed-gender populations using a variety of protocols. This study focused on a cohort of men who were predominantly intermediate risk. Two or more risk factors were present in 89% of the cohort. Completion of a standardized screening tool or cardiology consultation, as well as review by the nuclear medicine physician, likely diverted low-risk patients from MPI. All patients at this site underwent a single form of stress with regadenoson and technetium SPECT. In addition, FFR was incorporated in the assessment of lesion severity by LHC. Previous studies have focused on LHC correlation using a percentage of luminal stenosis as the only criterion for assessing lesion severity. Clinically, however, the discriminatory benefit of FFR in cases where lesion severity is uncertain often influences decision-making about revascularization.<sup>20</sup> Therefore, the identification of clinically significant stenosis in our study may be more representative of current practice.

Worldwide, current utilization of CSP MPI is limited. In some settings, this may be due to the availability of attenuation correction (AC). The incremental value of CSP MPI when AC is present has not been established—except for resolution of AC-related apical defects.<sup>21,22</sup> In a European survey, over 60% of centers do not utilize either AC or prone imaging.<sup>23</sup> In the United States, AC is still not available in many laboratories. One common argument against routine CSP MPI is that the extra <10 minutes per patient may impede workflow. Prone-only MPI is an alternative.<sup>24</sup> However, the diagnostic benefits of CSP MPI described here should not be extrapolated to prone MPI alone. By increasing the camera to chest wall distance, prone-only MPI has the potential to reduce overall counts in addition to the appearance of minor artifacts.<sup>4</sup> Two-position imaging provides two stress datasets and reduces the chance for motion.



**Figure 1.** Receiver-operating-characteristic curves for combined supine-prone (CSP, blue line) and supine-only (SU, orange line) myocardial perfusion imaging (MPI), compared to random chance (dotted reference line). The CSP area under curve of  $0.80 \pm 0.06$  is significantly larger than SU AUC of  $0.57 \pm 0.05$  ( $P = .004$ ) and is significantly different from random chance (AUC = 0.5,  $P < .001$ ). The SU MPI AUC does not differ significantly from the null hypothesis ( $P = .203$ ).

**Table 3.** Diagnostic accuracy of imaging protocols in obese LHC patients

Diagnostic test	SU MPI (N = 42)	CSP MPI (N = 30)	P value
Sensitivity (95% CI)	89% (65-99)	95% (74-99)	.167
Specificity (95% CI)	26% (10-48)	64% (31-90)	.034*
AUC $\pm$ SE	$0.58 \pm 0.06$	$0.79 \pm 0.08$	.030*

Sensitivity is expressed in terms of 95% CI and AUC is reported with standard error  
AUC, area under curve; CI, confidence interval; CSP MPI, combined supine-prone myocardial perfusion imaging; LHC, left heart catheterization; SE, standard error; SU MPI, supine-only myocardial perfusion imaging  
\* $P < .05$  is considered significant

This study highlights the marked reduction in equivocal interpretations using CSP MPI. A current quality benchmark has been limiting a laboratory's percentage of equivocal interpretations to 20% or less.<sup>19</sup> In this study, the use of CSP MPI reduced the number of equivocal interpretations from a borderline value of 18% to 4%—well below the recommended threshold. Additional data suggest there is improved inter-observer variability to CSP MPI.<sup>15</sup> The improved diagnostic certainty and diagnostic accuracy suggest a greater role for CSP MPI.

Whether that role should be confined to obese patients is unclear. A previous study by Berman et al

suggested that the diagnostic benefit of CSP MPI is independent of BMI.<sup>6</sup> Our artifact study demonstrates that reduction in attenuation artifact size was seen in both obese and non-obese patients. Despite a relatively small sample size of LHC patients, the obese subgroup of patients demonstrated significantly higher specificity and a high sensitivity with CSP imaging. In our smaller, non-obese subgroup who underwent LHC, the specificity benefit of CSP to SU MPI could not be established due to a small sample size. Although there was a possible reduction in sensitivity with CSP MPI, this has not been the case in larger cohorts.<sup>6</sup> The finding of artifact reduction in the prone vs supine position for non-obese patients would support further study of the diagnostic accuracy of CSP MPI in this group of men.

### LIMITATIONS

There were limitations to this study. First, this is an observational study and lacks the benefit of randomized design. Second, a common concern about prone imaging is that not all patients can tolerate it. We retrospectively calculated at 20% failure to prone rate, but the inability to prone and reason was not actively charted. In our experience, failure to prone was attributable to physical limitations of a patient. Other laboratories, however, report lower failure to prone rates in the 10% or less range. Also, only visual inspection for perfusion deficits on prone images, rather than quantification, was done because a normative prone database was not available. Visual analysis of CSP could contribute to the lower than expected specificity of CSP. Finally, in the cardiac catheterization correlation study, as mentioned previously, post-test referral bias is inherent.<sup>21,22</sup> Because few low risk patients were included, normalcy rates could not be obtained.

### CONCLUSION

Combined supine-prone MPI increases diagnostic certainty, reduces the size of diaphragmatic attenuation artifacts, and improves specificity for CAD detection in men. These diagnostic benefits are particularly apparent in obese men, and may support the routine use of the CSP MPI in these patients.

### NEW KNOWLEDGE GAINED

Combined supine/prone MPI improves diagnostic accuracy and diagnostic certainty in the men with CAD risk factors. The benefit was most apparent in obese men.

## Disclosure

*The authors report no conflicts of interest.*

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