

## The role of calcium score and CT angiography in the medical management of patients with normal myocardial perfusion imaging

Gaurav Choudhary, MD,<sup>a,b</sup> Victor Shin, MD,<sup>a,b</sup> Shahnaz Punjani, MD,<sup>a,b</sup>  
Nathan Ritter, MD,<sup>b</sup> Satish C. Sharma, MD,<sup>a,b</sup> and Wen-Chih Wu, MD<sup>a,b</sup>

**Background.** Individuals with normal myocardial perfusion imaging (MPI) may still have substantial coronary artery disease (CAD), which would benefit from aggressive medical therapy. The role of coronary artery calcium-score (CAC) and/or coronary CT Angiography (CTA) to identify additional treatment candidates in this population is unknown.

**Methods.** Ninety-four patients completed the study protocol and underwent CAC and CTA after MPI.

**Results.** In 81 patients who had a normal MPI, an algorithm using the clinical predictors, CAC, and then CTA was created to identify candidates for aggressive medical management; 24/81 patients had a high Framingham Risk Score (FRS) or diabetes, and need aggressive medical management, while 6/81 patients had a low FRS and low post-MPI probability of CAD. The use of CAC in 51/81 patients with intermediate clinical predictors would identify 23/51 patients with low risk (CAC < 100) and 11/51 patients (CAC > 400) for aggressive medical management. The remaining 17/51 patients with intermediate CAC scores (100-399) would require CTA, of which, would identify 8/17 additional patients with >50% stenosis for aggressive medical therapy.

**Conclusion.** A stepwise approach including history, CAC and CTA can identify about 50% of the patients with normal MPI who have a higher risk and may benefit from aggressive medical management. (J Nucl Cardiol 2010;17:45–51.)

**Key Words:** Myocardial perfusion imaging • SPECT • computed tomography (CT) • coronary artery disease • diagnostic and prognostic application • calcium score

---

**See related editorial, pp. 13–15**

---

### INTRODUCTION

Aggressive medical therapy for primary and secondary prevention of coronary artery disease (CAD) includes antithrombotic agents and control of serum cholesterol. The current guidelines from the National

Cholesterol Education Program, Adult Treatment Panel III (ATP III) recommend aggressive lipid-lowering therapy to a target serum LDL of <100 mg/dL for patients at high-risk for future cardiac events. Patients at the high-risk end of the spectrum include those with a 10-year event rate as predicted by Framingham Risk Scores (FRS) >20%, known coronary heart disease (CHD), or CHD risk equivalents. Coronary heart disease includes history of myocardial infarction, unstable angina, stable angina, coronary artery procedures (angioplasty) or bypass surgery, or evidence of clinically significant myocardial ischemia.<sup>1</sup>

Stress myocardial perfusion imaging (MPI) is the standard non-invasive method to detect and assess myocardial ischemia.<sup>2</sup> The presence of ischemia would classify the patients as having CHD and candidates for aggressive lipid management. However, a normal MPI in individuals without a previous cardiac history, does not necessarily rule out significant coronary stenosis or CAD burden which would benefit from aggressive medical therapy. In the recent years, a new imaging modality, the coronary artery calcium (CAC) score, has been identified

From the Vascular Research Laboratory,<sup>a</sup> Providence VA Medical Center, Providence, RI; Department of Medicine,<sup>b</sup> Warren Alpert Medical School of Brown University, Providence, RI.

Gaurav Choudhary and Victor Shin contributed equally to this work. Received for publication Jan 2, 2009; final revision accepted Oct 6, 2009.

Reprint requests: Gaurav Choudhary, MD, Vascular Research Laboratory, Providence VA Medical Center, 830 Chalkstone Ave., Providence, RI 02908, USA; [Gaurav\\_choudhary@brown.edu](mailto:Gaurav_choudhary@brown.edu).

1071-3581/\$34.00

Copyright © 2009 by the American Society of Nuclear Cardiology.

doi:10.1007/s12350-009-9158-x

as a possible adjunct to CAD burden estimation and risk stratification for targeting LDL goals.<sup>1,3</sup> In addition, multidetector cardiac computed tomography angiography (CTA) has also emerged as a new non-invasive modality to directly visualize coronary anatomy. There is abundant evidence supporting the correlation and accuracy of CTA with invasive coronary angiography and its use in the early detection of CAD.<sup>4</sup>

Since the current standard imaging modality for the non-invasive assessment of outpatients with suspected CAD is still stress MPI,<sup>2</sup> it is unclear if the addition of CTA or CAC to standard MPI testing would offer any additional benefit in the identification of high-risk candidates for aggressive medical management. The objective of this study is to evaluate the role of CTA and CAC, beyond clinical history alone, in identifying candidates with substantial CAD or CAD burden for aggressive medical therapy in patients without known CAD and normal stress MPI testing.

## METHODS

### Patient Sample

The institutional review board at the Providence VA Medical Center approved the registered protocol NCT00352937 ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)). Between March 2006 and August 2009, outpatients from the Providence VA Medical Center with no prior history of CAD, who were referred for stress MPI, were prospectively enrolled into the study. Patients were excluded if they had a previous history of an abnormal stress test, myocardial infarction, unstable angina, stable angina, PCI (angioplasty) or bypass surgery, or angiographic evidence of CAD based on invasive angiography. Other exclusion criteria were contraindications to CTA such as allergy to contrast dye, renal insufficiency (serum creatinine > 1.5 mg/dL), and pregnancy. Patients were also excluded if they were unable to perform a 20-second breath hold or if they had irregular rhythms that would prevent proper cardiac gating during image acquisition.

### Stress MPI

All patients underwent same day (under 200 lbs) or a 2-day (over 200 lbs) stress-rest Technetium-99m tetrophosmin gated MPI using the standard Bruce treadmill or dipyridamole infusion protocols.<sup>2</sup> Data were acquired with a dual-head SPECT camera (ECAM Signature, Siemens) and images were analyzed using 4DM SPECT (Ann Arbor, MI) by the MPI reader of the day (three experienced readers at Providence VA Medical Center) unaware of the study procedures. The stress test was considered abnormal if images revealed perfusion defects consistent with infarct or ischemia.

### CTA Protocol

CTA was performed within 2-4 weeks after the stress test. Intravenous metoprolol was administered to achieve a target

heart-rate <60 beats/min. One sublingual nitroglycerin tablet (0.4 mg) was given immediately prior to the scan. All studies were performed using a multi-detector computed tomography 16-slice scanner (Lightspeed 16, GE), with a gantry rotation time of 500 ms and temporal resolution of 250 ms. Images were acquired through retrospective gating at a slice collimation of 16 × 0.625 mm. Tube current ranged from 300 to 440 mA at 120 kV depending on preset parameters that increased current and table pitch based on body weight.

An initial scout scan of the cardiac region was performed followed by a timing bolus scan using a 20 mL test bolus of non-ionic contrast (Visipaque, GE). The actual CTA was performed using a dual-bolus injector that delivered an initial bolus consisting of 60 mL of 100% contrast, followed by a 60 mL mixture of 60% contrast and 40% saline, and then followed by 50 mL saline. The total contrast volume for each patient was approximately 116 mL including the timing bolus.

Initial data sets were reconstructed at 70%, 75%, and 80% of the RR interval and transferred to a workstation for analysis (CardIQ<sup>®</sup> Analysis, Advantage Workstation 4.2<sup>®</sup>, GE). Two experienced cardiologist readers, blinded to results of the nuclear stress test, identified and analyzed the coronary anatomy using the 17-segment modified AHA classification. All segments greater than 1.5 mm in diameter were evaluated with regards to severity of luminal stenosis. Each segment was classified as minimal to no visible luminal stenosis, mild-moderate CAD (luminal stenosis <50%), or substantial CAD (>50% luminal stenosis) by consensus of the readers.

### CAC Scoring

Coronary artery calcium scoring was performed using the Agatston method on the gated non-contrast images acquired prior to CTA (scout scan) at 2.5 mm slice thickness and analyzed using GE Advantage Workstation 4.2<sup>®</sup> Smartscore<sup>®</sup> software. Each vessel was scored independently and a cumulative score was then calculated. Patients were considered to have minimal to no CAD burden if their CAC was <100, mild-moderate CAD burden if the CAC was 100-399, and substantial CAD burden if CAC was ≥400.

### Data Analysis

Based on the ATP III and ACC/AHA guidelines, we first determined the future risk of cardiac events and the post-MPI probability of CAD.<sup>1</sup> Post-test probability was estimated using Bayesian analysis where post-test odds = pretest odds × (1 – sensitivity)/(specificity), and post-test probability = post-test odds/(post-test odds + 1).<sup>5</sup> Pretest probability for CAD was estimated using the Diamond and Forrester algorithm.<sup>6</sup> The sensitivity and specificity of exercise MPI were extracted from the current ACC/AHA guidelines as 87% and 73%, respectively; while those for dipyridamole MPI were 89% and 75%, respectively.<sup>2</sup>

To assess the relationship between the CAC and CTA, CAC were compared among patients with minimal to no CAD, with mild to moderate CAD and with substantial CAD by CTA

using one-way ANOVA. The degrees of CAD burden (minimal to none, mild to moderate, and substantial) as measured by CAC were then correlated with the severity of luminal stenosis by CTA with Pearson’s test.

In order to elucidate how CAC and CTA fit into the current CAD management, we tabulated the CAC and CTA results (to either CAC > 400 or CTA with stenosis >50% or both) according to the future risk of cardiac events (low, intermediate, or high) and the post-MPI probability of CAD (low or intermediate) in a 3 × 5 table. High-risk candidates that may benefit from aggressive medical management were identified based on a high risk of future cardiac events per the ATP III criteria, those with a substantial CAD burden (CAC ≥ 400 mg/dL) and those with substantial CAD (luminal stenosis >50%) by CTA. A step wise algorithm incorporating the patient’s ATP III risk assessment and post-MPI probability of CAD, CAC, and CTA, was then built based on the premises of identification of high-risk candidates while minimizing the use of additional imaging technology such as CAC and/or CTA.

## RESULTS

A total of 126 patients were prospectively enrolled, but 30 patients withdrew prior to undergoing MDCT (six of whom had abnormal MPI scans). Of the 96 patients who underwent CAC and CTA after their MPI, two patients could not complete the protocol due to technical difficulties (one patient had an inadequate bolus and subsequently developed dye allergy, and the other had difficult IV access). Ninety-four patients successfully completed the study protocol. Ten of the 94 patients had a submaximal stress test that were negative for ischemia or infarct by MPI; three of whom had both a CAC ≥ 400 and substantial CAD on CTA, and seven patients had CAC scores <400, three of whom had substantial CAD and four had mild-moderate CAD on CTA. Of the 84 diagnostic MPI’s, three patients had an abnormal MPI scan, their CAC scores were 296, 358, and 1,701, respectively, and their CTA showed substantial CAD (Figure 1).

### Demographics

Eighty-one patients with a diagnostically normal MPI were the focus of this study and their baseline characteristics are shown in Table 1. The majority of patients was men with a mean age of 60 years. Forty-eight patients underwent Bruce protocol, while 33 received dipyridamole infusion during their stress MPI.

Based on the ATP III criteria, 18 patients (22%) were classified as having a low 10-year risk for CHD events, 55 patients (68%) had moderate risk, and 8 patients (10%) were at high risk. Most patients presented with an intermediate post-test probability for significant CAD after their MPI. Sixty-three percent (n = 51) of all

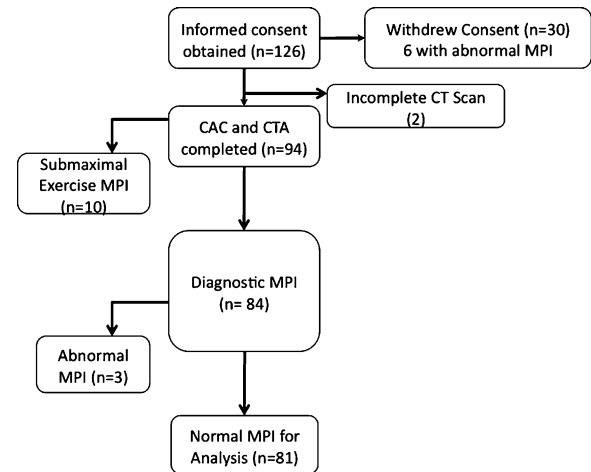


Figure 1. Flowchart of study enrollment.

Table 1. Patient demographics

| Clinical characteristics (n = 81)   |            |
|-------------------------------------|------------|
| Gender (m/f)                        | 77/3       |
| Age (yrs) ± SD                      | 60.4 ± 9.6 |
| Risk factors                        |            |
| Diabetes mellitus                   | 17 (21%)   |
| Hypertension                        | 47 (58%)   |
| Dyslipidemia                        | 56 (69%)   |
| Family history                      | 29 (36%)   |
| Current smoking                     | 29 (36%)   |
| Symptoms                            |            |
| No symptoms                         | 15 (19%)   |
| Dyspnea                             | 11 (14%)   |
| Atypical chest pain                 | 46 (57%)   |
| Typical chest pain                  | 9 (11%)    |
| Post-MPI CAD probability assessment |            |
| Low (<15%)                          | 31 (38%)   |
| Intermediate (15–85%)               | 50 (62%)   |
| ATP III 10-year cardiovascular risk |            |
| Low (<10%)                          | 18 (22%)   |
| Intermediate (10–20%)               | 55 (68%)   |
| High (>20%)                         | 8 (10%)    |

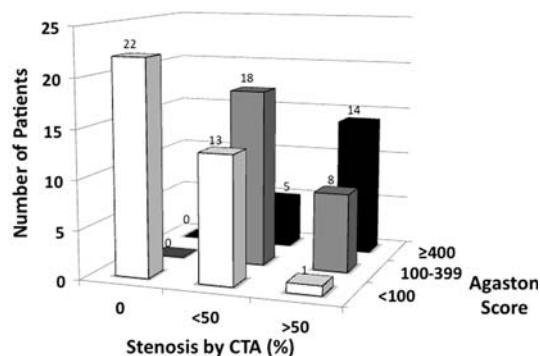
patients had either an intermediate 10-year FRS event risk or an intermediate post-MPI probability of CAD.

### Imaging Results

CTA revealed that 22 patients (27%) had minimal to no luminal CAD, 36 patients (44%) had mild-moderate disease in at least one coronary segment, and 23 patients (28%) had substantial (>50% stenosis) disease. Among patients with abnormal CTA results, the number of disease segments ranged from 1 to 7 for those with

mild-moderate CAD and 1 to 10 for those with substantial CAD. The average number of evaluable segments per patient was 13 out of 17. Twenty-four (30%) patients had at least 1 unevaluable segment due to excessive motion.

The CAC of the study population ranged from 0 to 2,701. Thirty-six patients (44%) had a CAC < 100 (16 of which had a CAC of zero), 26 patients (32%) had a CAC between 100 and 399, and 19 patients (23%) had a CAC equal or greater than 400. The mean CAC's differed according to the CAD severity as assessed by CTA. They were  $4.9 \pm 14.2$  for patients with minimal to no luminal CAD,  $219.5 \pm 247.5$  for those with mild to moderate luminal CAD, and  $801.1 \pm 767.3$  for patients with substantial luminal CAD ( $P < .01$ ). Conversely, in patients with a minimal to no CAD burden by CAC, only one patient had a >50% stenosis on CTA, suggesting a negative predictive value of 97% for detection of substantial luminal coronary stenosis. In the group of patients with a CAC of zero, only one out of 16 patients had CTA-discernible CAD, which was mild-moderate in severity. Similarly, 14 out of 19 patients with a substantial CAD burden by CAC had >50% stenosis on CTA, and the other five patients had <50% stenosis on CTA suggesting a positive predictive value of 74% for detection of substantial CAD. In the group with mild to moderate CAD burden by CAC, the likelihood of substantial CAD by CTA was 31% (Figure 2). The correlation between the degree of CAD burden estimated by CAC and severity of luminal stenosis observed by CTA was excellent,  $r = .73$ ,  $P < .01$ .



**Figure 2.** Distribution of patients with normal myocardial perfusion imaging stratified by coronary stenosis on CT angiography, and Agastson calcium score (n = 81). There is one patient with a CAC < 100 and a CAD with >50% stenosis by CTA. However, this patient had a 10-year event risk >30% which would have qualified him as high risk of future events and candidate for aggressive medical management. No patients with CAC = 0 had CAD > 50% stenosis by CTA.

### ATP III Risk, Post-test Probability, CAC and CTA for Identification of High Risk Candidates

Table 2 shows the distribution of CAC and CTA results stratified by 10-year event risk and post-MPI probability of CAD in patients with normal MPI. Twenty-four patients (30%) had a high ATP III risk or diabetes. Fifteen out of those 24 patients had either a substantial CAD burden by CAC or a substantial CAD by CTA, with six patients having both. Of the 51 patients (63%) with either an intermediate 10-year FRS event risk or an intermediate post-test probability of CAD, 11 had substantial CAD burden by CAC and 16 had substantial CAD by CTA, with eight of them having both. In the six patients (7%) who had a both low 10-year event risk and a low post-test probability, none had a CAC  $\geq 400$  or >50% stenosis in CTA.

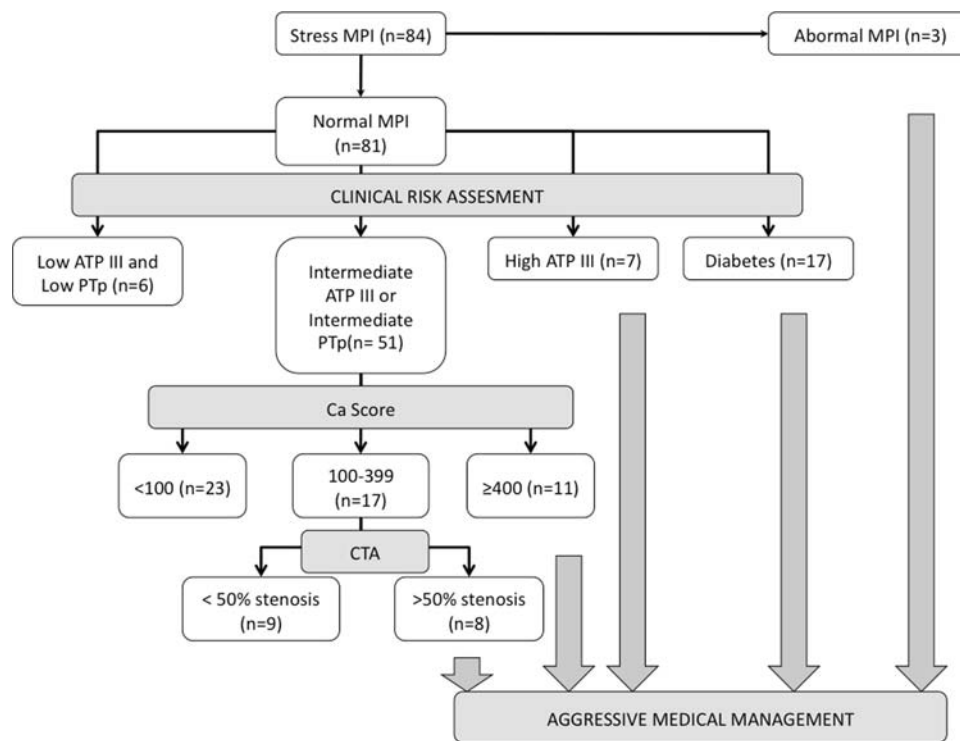
Based on the above data, an algorithm using the clinical predictors (ATP III 10-year event risk and post-MPI probability for CAD), CAC and CTA results were created to identify high-risk individuals with normal MPI that may benefit from aggressive medical management while minimizing the use of CAC or CTA whenever feasible (Figure 3). The first step of the algorithm would include clinical risk stratification using both ATP III risk and post-MPI probability of CAD, which would have identified 24 patients (30%) with high ATP III risk or diabetes as candidates for aggressive therapy and six patients (7%) with low ATP III risk and low post-test probability who would not require further studies for risk assessment. The second step would be performing CAC focusing on the group of patients with either an intermediate ATP III risk or intermediate post-MPI probability of CAD (n = 51 or 63% of patients). A CAC of either  $\geq 400$  (n = 11) or <100 (n = 23) would eliminate the need to proceed to CTA since it would have identified or excluded the candidates for aggressive medical therapy, respectively. The third step would consist of CTA on patients with an intermediate ATP III risk or intermediate post-MPI probability of CAD and a mild-moderate CAC (n = 17 or 21% of patients). The addition of CTA would have identified 8 out of 17 patients with substantial luminal stenosis who might benefit from aggressive medical management.

### DISCUSSION

Myocardial perfusion imaging is one of the most frequently used non-invasive tests to diagnose CAD and ischemia. The presence of ischemia on MPI suggests high risk and is used by the ATP III guidelines as an indicator of presence of CHD.<sup>1</sup> If the MPI study is normal, in general the risk of significant adverse

**Table 2.** Distribution of high CAC and significant stenosis on CTA stratified by FRS and post-test probability

| FRS              | Post-test probability | N  | CAC > 400 | Stenosis > 50% (CTA) | Both high CAC and significant stenosis |
|------------------|-----------------------|----|-----------|----------------------|----------------------------------------|
| Low              | Low                   | 6  | 0         | 0                    | 0                                      |
| Low              | Intermediate          | 8  | 0         | 3                    | 0                                      |
| Intermediate     | Low                   | 18 | 5         | 4                    | 3                                      |
| Intermediate     | Intermediate          | 25 | 6         | 9                    | 5                                      |
| High or diabetes |                       | 24 | 8         | 7                    | 6                                      |
| Total            |                       | 81 | 19        | 23                   | 14                                     |



**Figure 3.** Proposed algorithm that may be used in stepwise risk stratification of patients who present for stress myocardial perfusion testing. The numbers in parentheses refer to the number of patients in this study that fall into the particular category. *MPI*, Myocardial perfusion imaging; *ATP III*, 10-year event risk as predicted by Framingham risk score; *PTp*, Post-test probability of having significant coronary artery disease; *CTA*, CT Angiography.

(cardiac) events is reported as <1% per year in absence of co-morbidities, about 1% per year in the presence of angiographically documented CAD, and between 1% and 2% per year in the presence of significant co-morbidities.<sup>7-9</sup> Hence, it has been suggested that for choosing therapeutic interventions in patients with normal scans, consideration be given to their clinical history and risk factors.<sup>7,9</sup>

The presence of increased CAC has been shown to correlate with the presence of significant CAD independent of traditional risk factors<sup>10</sup> as well as increased risk of adverse cardiovascular events.<sup>3</sup> Pooled data show that in an intermediate risk population as classified by clinical characteristics, CAC can be useful in further risk stratification. In this group, patients with <100, 100-399, and ≥400 Agatston score had an annual risk of CHD death

and MI of 0.4%, 1.3%, and 2.4%, respectively.<sup>3</sup> In addition, CTA has been shown to be an accurate diagnostic procedure for CAD.<sup>11</sup> Recent studies have demonstrated that CTA can also be used as a prognostic tool for prediction of adverse cardiac event<sup>12-14</sup> that is incremental and independent of traditional risk factors and CAC.<sup>13</sup> The highest risk CTA is those associated with >50% stenosis in one of the major coronary vessels, while the prognosis of patients with no detectable stenosis is reportedly excellent. Hence, a high CAC and/or significant stenosis on CTA would both suggest a patient to be at increased risk for adverse cardiac events and a potential candidate for aggressive cardiovascular risk reduction. Since the population studied in CAC and CTA reports shared similar characteristics as those patients being referred for MPI testing, our study provided insight on the potential role of these techniques in the diagnosis and management of substantial CAD or CAD burden that would have been otherwise undiscovered in this population.

As noted by others,<sup>15-18</sup> we found a substantial number of patients with a normal MPI to have a CAC score >100 and significant CAD noted on CTA. By adding CTA after a normal MPI, we identified 20% of patients with substantial luminal stenosis in absence of diabetes and a calculated FRS 10-year event risk of <20%, who could benefit from aggressive medical therapy. However, CTA is associated with increased risk of radiation and contrast exposure compared to CAC. By using the stepwise algorithm proposed, we could have identified all these patients by performing a CAC in 63% of patients and performing a CTA in only 21% of the patients. Hence, the proposed algorithm would have minimized the radiation and contrast exposure to the patient, as well as reduced cost of extra testing, while identifying all the high-risk patients for aggressive medical management. With the availability of new SPECT-CT scanners, it is conceivable that the utilization of multimodality imaging will rise. Our study shows how these new technologies can have a role in addition to the clinical history in assessing the risk of patients with normal MPI. An alternative strategy could include use of CAC alone and consider all patients with a score >100 as potential candidates of aggressive therapy. However, such an approach will include 21% more patients as candidates of aggressive medical therapy (i.e., those with CAC 100-399 and <50% stenosis) compared to the stepwise approach using CTA. Future studies with outcomes and cost-effectiveness of either approach will be required to choose the optimal diagnostic algorithm.

In this study, we also evaluated whether adding post-MPI probability for CAD to the ATP III risk assessment increased the discriminatory role of clinical history in identifying high-risk candidates who would

benefit from aggressive medical treatment. The results are encouraging, since incorporating post-MPI probability for CAD into our proposed algorithm we identified an additional group of patients in low FRS risk but intermediate post-test probability with a 38% incidence of substantial coronary stenosis by CTA. This group likely behaves as an intermediate risk category rather than low risk as determined by ATP III risk assessments.

Our study has several limitations. First, the study enrolled predominantly male patients at a single-center who were referred for stress MPI by a multi-specialty group of physicians and may not represent the practice pattern of the general population. However, stress MPI is one of the most commonly used technique for diagnosis of CAD both locally and nationwide,<sup>7</sup> and hence our referral pattern is unlikely to be different than that of the rest of the country. Second, the MDCT scan was performed using a 16-slice scanner instead of the newer 64-slice scanner. However, the sensitivity and specificity of per-segment analysis of all evaluable segments has been reported as 98% for 16-slice CT scanner compared to 97% for the 64-slice scanner, and the specificity is comparable at 96%.<sup>11</sup> The number of unevaluable segments for the 16-slice scanner are higher than the 64-slice scanner.<sup>19</sup> We minimized the number of segments with motion artifact in our population by aggressively controlling the heart rate at the time of scan. Lastly, we do not have the prognosis data associated with the study population at this time. However, the event risks associated with FRS, post-test probability, CAC and CTA are robust and have been well documented in previous studies and can be used as a surrogate to the risk that would be associated with our patient population. Our results can aid the risk stratification of patients with normal MPI who may not be at low-risk.<sup>7</sup> Further prospective study is needed to test whether addition of biomarkers, may further reduce the number of patients who would need to undergo CAC or CTA, thereby minimizing radiation exposure as well as the cost. We continue to follow these patients and hope to report the prognosis data in the future.

In summary, we report that the use of clinical risk predictors, CAC and CTA in patients with normal stress MPI can be a useful adjunct to identify patients with significant coronary artery disease who may benefit from aggressive medical management. Moreover, by using a stepwise risk stratification model, we can minimize the number of CTA that will be needed for this purpose.

## Acknowledgments

*This material is based upon work supported by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development: Targeted Research Enhancement*

*Program Grant (TRP 04-179) from the Health Services Research and Development Service (W-CW); Biomedical Laboratory Research and Development Service (CDA-2 Award to GC). The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs.*

## References

1. National Cholesterol Education Program (NCEP) Expert Panel on Detection E, Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002; 106(25):3143-421.
2. Klocke FJ, Baird MG, Lorell BH, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Cardiac Radionuclide Imaging). *J Am Coll Cardiol* 2003;42(7):1318-33.
3. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol* 2007; 49(3):378-402.
4. Achenbach S. Computed tomography coronary angiography. *J Am Coll Cardiol* 2006;48(10):1919-28.
5. Detrano R, Yiannikas J, Salcedo EE, et al. Bayesian probability analysis: A prospective demonstration of its clinical utility in diagnosing coronary disease. *Circulation* 1984;69:541-7.
6. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. *N Engl J Med* 1979;300:1350-8.
7. Berman DS, Shaw LJ, Hachamovitch R, et al. Comparative use of radionuclide stress testing, coronary artery calcium scanning, and noninvasive coronary angiography for diagnostic and prognostic cardiac assessment. *Semin Nucl Med* 2007;37:2-16.
8. Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). *Circulation* 2003;107:149-58.
9. Hachamovitch R, Hayes S, Friedman JD, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: What is the warranty period of a normal scan? *J Am Coll Cardiol* 2003;41:1329-40.
10. Ho JS, Fitzgerald SJ, Stolfus LL, et al. Relation of a coronary artery calcium score higher than 400 to coronary stenoses detected using multidetector computed tomography and to traditional cardiovascular risk factors. *Am J Cardiol* 2008;101:1444-7.
11. Janne d'Othée B, Siebert U, Cury R, Jadvar H, Dunn EJ, Hoffmann U. A systematic review on diagnostic accuracy of CT-based detection of significant coronary artery disease. *Eur J Radiol* 2008;65: 449-61.
12. Pundziute G, Schuijf JD, Jukema JW, et al. Prognostic value of multislice computed tomography coronary angiography in patients with known or suspected coronary artery disease. *J Am Coll Cardiol* 2007;49:62-70.
13. Ostrom MP, Gopal A, Ahmadi N, et al. Mortality incidence and the severity of coronary atherosclerosis assessed by computed tomography angiography. *J Am Coll Cardiol* 2008;52:1335-43.
14. Gaemperli O, Valenta I, Schepis T, et al. Coronary 64-slice CT angiography predicts outcome in patients with known or suspected coronary artery disease. *Eur Radiol* 2008;18:1162-73.
15. Schuijf JD, Wijns W, Jukema JW, et al. A comparative regional analysis of coronary atherosclerosis and calcium score on multislice CT versus myocardial perfusion on SPECT. *J Nucl Med* 2006;47:1749-55.
16. Scholte AJ, Schuijf JD, Kharagitsingh AV, et al. Different manifestations of coronary artery disease by stress SPECT myocardial perfusion imaging, coronary calcium scoring, and multislice CT coronary angiography in asymptomatic patients with type 2 diabetes mellitus. *J Nucl Cardiol: Am Soc Nucl Cardiol* 2008;15: 503-9.
17. Budoff MJ, Rasouli ML, Shavelle DM, et al. Cardiac CT angiography (CTA) and nuclear myocardial perfusion imaging (MPI)—a comparison in detecting significant coronary artery disease. *Acad Radiol* 2007;14:252-7.
18. Gaemperli O, Schepis T, Valenta I, et al. Functionally relevant coronary artery disease: Comparison of 64-section CT angiography with myocardial perfusion SPECT. *Radiology* 2008;248:414-23.
19. Stein PD, Beemath A, Kayali F, Skaf E, Sanchez J, Olson RE. Multidetector computed tomography for the diagnosis of coronary artery disease: A systematic review. *Am J Med* 2006;119:203-16.