Integrated Coronary Computed Tomographic Angiography in an Office-Based Cardiology Practice

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Multidetector coronary computed tomographic angiography (CCTA) visualizes coronary artery disease directly, thereby identifying atherosclerosis rather than ischemia. CCTA has the potential to be a useful, noninvasive gatekeeper for the identification of patients who are appropriate candidates for conventional coronary angiography and can also help determine the need for more aggressive risk modification, including cholesterol control. Integration of 64-slice CCTA scanning into a large, urban cardiology practice resulted in clearer stratification of patients into those with and without disease. Physicians used this information to improve lipid management while simultaneously reducing the use of other cardiac testing. The ability to assess cardiac calcium scoring was an additional advantage of integrating CCTA into the practice. Further reductions in the use of myocardial perfusion imaging may be expected as a result of the use of CCTA as the first test for the intermediate-risk patient.

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The morbidity, mortality, and economic costs associated with coronary artery disease (CAD) have stimulated the development of noninvasive risk stratification methods to identify patients for interventions directed toward reducing the risk of CAD-related events. One potential such noninvasive method is 64-slice multidetector coronary computed tomographic angiography (CCTA), which visualizes CAD directly, thereby identifying atherosclerosis rather than ischemia.[1] Studies comparing 64-slice CCTA to invasive coronary angiography as the gold standard have reported high sensitivity to detect hemodynamically relevant stenoses, high specificity to correctly identify the absence of stenoses, and high negative predictive value.[2-6] The high specificity and negative predictive value of 64-slice CCTA, combined with the ability to measure a calcium score for prognostic purposes and characterize plaque not seen with any other noninvasive technology, raises the likelihood that clinicians will use this technique in intermediate-risk patients, including those who smoke or who have elevated blood pressure, high cholesterol, diabetes, chest pain, or similar variables. CCTA has the potential to be a useful, noninvasive gatekeeper for the identification of patients who are appropriate candidates for conventional coronary angiography and can also help determine the need for more aggressive risk modification, including cholesterol control.[7] CCTA may become yet another approach in an increasing crowd of recommended tests that act as an entry point to evaluate the cardiac patient, joining the cardiac calcium score (CCS), carotid intima-media thickness (IMT), and a plethora of metabolic factors and risk scales, including the Framingham risk score.

Despite this potential, it has been challenging to determine the effect of 64-slice CCTA on patient care outside of a controlled research environment because computed tomography (CT) is usually based in hospitals or diagnostic imaging centers, with referrals from multiple sources and the associate difficulty in determining follow-up and details of multimodality testing. However, the Cardiovascular Medical Group of Southern California (CVMG), an urban referral and primary care cardiology practice with 17 cardiologists and a base of 40,000 active patients, recognized that the evaluation of the cardiac patient might undergo a major shift as a result of CCTA technology and installed a 64-slice CCTA scanner onsite in August 2005. This unique environment has allowed analysis of the effects of CCTA when it was made available to patients and integrated into the office practice. To assess the impact of CCTA on cardiology patients at CVMG, a retrospective analysis was performed based on 1-year follow-up of the first 100 patients evaluated onsite using 64-slice CCTA with regard to cholesterol management. Data were gathered to document patient outcomes and assess how practice patterns changed for evaluation of CAD in intermediate-risk patients with regard to other cardiac testing in comparison with all patients who were studied in the same year.

Methods

Practice Pattern Observation: General

In January 2006, cardiologists in the CVMG practice first had CCTA as well as general CT available for routine primary and cardiac care. CCTA was performed only in patients who were considered to be at intermediate risk as judged by the referring cardiologist based on the presence of risk factors. General CT was also performed as required for noncardiac primary care indications.

A retrospective review of electronic practice records was undertaken to identify the pattern of testing in the 6 months prior to the introduction of CCTA. All noninvasive cardiac tests for CAD diagnosis and management were identified, including myocardial perfusion scintigraphy, stress echocardiography, and exercise electrocardiography. These data were compared with those from the testing practice within the group in the first and second 6-month time periods following the availability of CCTA within the practice.

Practice Pattern Observation: Subset Analysis of Post-Test Lipid Level Change

Detailed information regarding CAD and lipid profiles was recorded for the first 100 consecutive patients who underwent CCTA. Clinical interpretations by 4 experienced cardiologists were reviewed and patient "disease type" was defined on the basis of clinical records as either no/insignificant CAD, new CAD (defined as $\geq$ 25% luminal narrowing and/or significant mixed or noncalcified plaque), or existing disease (prior abnormal invasive coronary angiography or known myocardial infarction). Patients were also defined as having either calcified coronary plaque (Hounsfield units [HU] $\geq$ 130), noncalcified plaque (HU $<$ 130), or mixed plaques. Lipid levels measured prior to and up to 1 year following the CCTA evaluation were recorded. Subgroup analysis was performed for those patients with total cholesterol exceeding 200 mg/dL or low-density lipoprotein (LDL) cholesterol exceeding 130 mg/dL.

CCTA Method

Only patients in sinus rhythm without contraindication to iodinated contrast agents were included in the study. All patients routinely received 50 or 100 mg of oral metoprolol prior to the procedure and underwent oral hydration. If the heart rate was still higher than 60 beats/min, additional intravenous (IV) metoprolol was administered. Patients received nitroglycerine spray (0.4 μg). CCTA was performed using the 64-slice CCTA (LightSpeed® VCT 64-Slice Scanner; GE Healthcare, Buckinghamshire, United Kingdom) with a 64 mm $\times$ 0.625 mm collimation and a gantry rotation time of

375 milliseconds. A tube voltage of 120 kV to 140 kV was applied according to the patient's body weight. A double-bolus protocol was used. Image data sets were analyzed using volume rendering, multiplanar reconstruction, and vessel analysis software packages (Advantage Workstation 4.3, GE Healthcare). CCS was assessed with a dedicated software application (SmartScore, GE Healthcare), and an Agatston score was recorded for each patient.

Data Analysis
For the first 100 consecutive patients in 2006, a database was constructed that included patient age and sex; pre-CCTA and post-CCTA total cholesterol, LDL cholesterol, and high-density lipoprotein (HDL) cholesterol levels (binned into 3-month periods); and cardiac CCTA results (CCS, presence or absence of CAD, and presence or absence of mixed plaque). Descriptive statistics were obtained. Continuous variables were expressed using both the median and mean values and compared using a 1-tailed paired student's *t* test, and categorical variables were expressed as frequencies. A *P* value of less than .05 was considered significant. All statistical analyses were performed using Statistical Package for the Social Sciences software, version 15.0 (SPSS Inc., Chicago, IL).

Results

Practice Pattern Observation: General
During the period from January 2006 to December 2006, a total of 3468 patients underwent 3927 onsite CT examinations. On average, each patient underwent 1.2 CT-based studies. Overall, 2042 (52%) patients underwent contrast studies, including aortic, carotid, and peripherals, and 624 (18%) had only a CCS assessment. Noncardiac CT, including chest, brain, abdominal, pelvic, and other miscellaneous studies, was performed in 48% of patients. A comparison of CCTA and other noninvasive cardiac tests performed in the practice from 6 months before through 12 months after implementation of CCTA is depicted in Figure 1. During the 6 months prior to the availability of CCTA, 1682 myocardial perfusion scintigraphy studies were performed; after CCTA became available, the number of nuclear scans decreased by 14% (to 1442) in the first 6-month period and by 15% (to 1422) in the second 6-month period. Over the same period, the number of treadmill tests decreased by nearly 50% (from 240 to 149), and the number of exercise echocardiograms increased slightly (from 531 to 589).

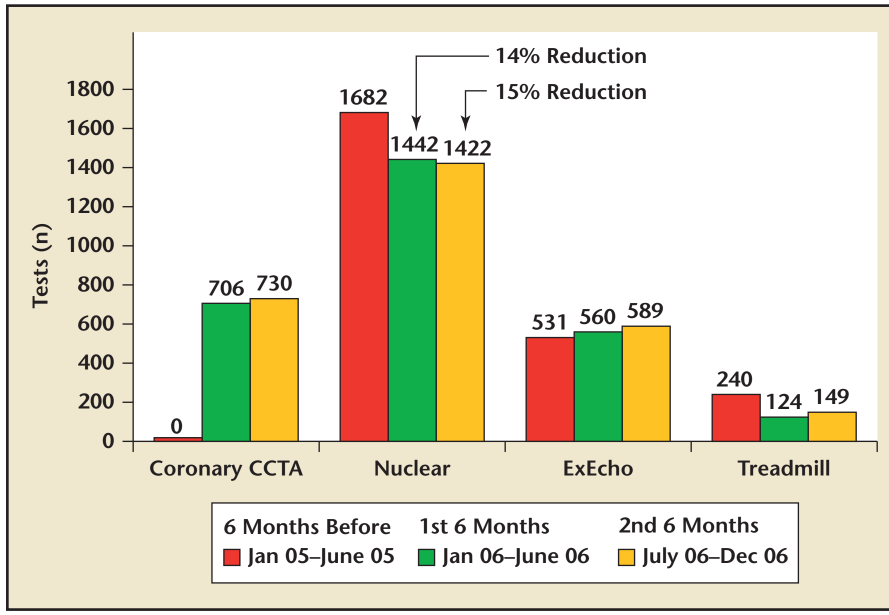

Figure 1. *A comparison of CCTA and other noninvasive cardiac tests performed in the practice from 6 months before through 12 months after implementation of CCTA. CCTA, cardiac computed tomographic angiography; ExEcho, exercise electrocardiography.*

Practice Pattern Observation: Subset Analysis of Post-Test Lipid Level Changes
The results of cardiac CCTA evaluations for the first 100 patients were categorized according to the presence or absence of CAD (Table 1). Among these patients, 41 had existing CAD, 33 were diagnosed with new disease, and 26 had no significant disease. The median CCS score was 280 (range: 0-6527) and was markedly higher for patients with existing CAD (1010) than for "new disease" patients (277) and for the subset of patients with only plaque (noncalcified or mixed) (207). Among the 14 patients who had hyperlipidemia (defined as total cholesterol at or exceeding 200 mg/dL) prior to CCTA, the median CCS was 252, with a wide range (0-2583). In comparison, patients without CAD had a median CCS of 0 and a total cholesterol of 167 mg/dL.

Serum Lipid Tests
Results of serum lipid tests, including total cholesterol, HDL cholesterol, and LDL cholesterol, were available prior to and following CCTA examination for 58 patients. (Patients with incomplete data were not included in this analysis.) Group mean pre-CCTA and post-CCTA lipid levels and

Table 1
Results of Cardiac CCTA Evaluations for the First 100 Patients

Characteristic	Normal (n = 26)	New CAD (n = 33)	Existing CAD (n = 41)	Total (n = 100)	Plaque Subset* (n = 20)
CCS					
Number tested	26	33	41	100	20
Median	0	277	1010	280	207
Range (min-max)	0-211	0-3900	0-6527	0-6527	0-3900
Percent patients with:					
CCS 0	69.2%	3.0%	2.4%	20.0%	10.0%
CCS 1 to 100	23.1%	27.3%	0%	15.0%	25.0%
CCS 101 to 400	7.7%	33.3%	19.5%	21.0%	40.0%
CCS > 400	0%	36.4%	78.0%	44.0%	25.0%
Vessel Obstruction					
Number tested	26	33	41	100	20
% ≥ 25% obstruction/plaque	0	100	100	74	19
Ejection Fraction by CCTA					
Number tested	22	26	35	83	15
Median	63.5	64.0	64.0	64.0	64.0
Range (min-max)	(46-72)	(11-82)	(21-83)	(11-83)	(54-80)

*Includes 16 new CAD, 3 existing CAD, and 1 normal patient.
CCTA, cardiac computed tomographic angiography; CAD, coronary artery disease; CCS, cardiac calcium score.

changes for these patients (matched pairs) are presented in Table 2 (categorized according to the CCS obtained during CCTA examination) and Table 3 (categorized by patient disease type). Following CCTA examination, there were significant decreases in group mean total cholesterol among patients with a CCS exceeding 100, but not among patients with a lower CCS. Among patients with a CCS between 100 and 400, there was a significant decrease in LDL. No significant change was observed in LDL levels among patients with a CCS exceeding 400, whose baseline mean LDL level was already low (87 mg/dL), possibly due to treatment. (The reduced follow-up level of 81 mg/dL did not reach statistical significance.)

Among patients defined as having any noncalcified plaque by CCTA, the mean pretest LDL level was 119 mg/dL, and mean pretest total cholesterol was 181 mg/dL. Following performance of CCTA in these patients, there was a significant decrease in mean LDL (from 119 mg/dL to 96 mg/dL [P = .011]), as well as a decrease in total cholesterol that approached statistical significance (181 mg/dL to 160 mg/dL [P = .054]). In the 11 patients with baseline total cholesterol at or exceeding 200 and the 9 patients with baseline LDL at or exceeding 130, significant decreases in total and LDL cholesterol levels were observed following performance of CCTA (Table 3).

Discussion

CCTA was rapidly adopted into the practice for both noncardiac and cardiac assessments. The utilization of noncardiac CT within a cardiac practice would be expected to vary with the amount of primary care that is conducted there, which becomes an important consideration in determining whether CT is an economic option. In this analysis, utilization was limited to 1.2 studies per patient, which supports the notion that CT can be integrated into a private, primary cardiac care urban practice without overutilization with regard to simultaneous multiorgan use.

The ability to assess the CCS was an additional advantage of integrating CT into the practice. The CCS has been proposed as a reasonable first-line test for the intermediate-risk patient and for possible use even as a screening study, adding prognostic information that complements or better predicts outcomes than standard

Table 2
Comparison of Pre- and Post-CCTA Lipid Levels by CCS

Characteristic	CCS 0 (n = 8)	CCS 1-100 (n = 10)	CCS 101-400 (n = 13)	CCS > 400 (n = 27)	Total (n = 58)
Total Cholesterol, Mean					
Pre-CCTA (mg/dL)	172.88	174.70	181.15	161.33	169.67
Post-CCTA (mg/dL)	156.75	173.90	147.69	146.67	152.98
Change (%)	−9.33	−0.46	−18.47	−9.09	−9.84
Significance	NS	NS	**.015**	**.006**	**.000**
LDL Cholesterol, Mean					
Pre-CCTA (mg/dL)	109.59	112.73	116.86	87.35	100.41
Post-CCTA (mg/dL)	97.75	100.4	93.15	81.04	89.40
Change (%)	−10.80	−10.94	−20.29	−7.22	−10.97
Significance*	NS	NS	**.03**	NS	**.002**
HDL Cholesterol, Mean					
Pre-CCTA (mg/dL)	44.00	51.1	46.62	48.59	47.95
Post-CCTA (mg/dL)	40.63	52.0	40.54	48.33	46.16
Change (%)	−7.66	1.76	−13.04	−0.54	−3.73
P Value	**.02**	NS	**.048**	NS	NS

*Paired *t* tests are 1-tailed.
CCTA, cardiac computed tomographic angiography; CCS, cardiac calcium score; LDL, low-density lipoprotein; HDL, high-density lipoprotein; NS, not significant.

clinical risk factors.[8-11] Notably, in this study, a CCS above 100 was associated with physician treatments that resulted in significant reduction in LDL despite normal baseline LDL levels in this group. A trend toward lower LDL post-CCTA was also present for patients with a CCS below 100, but this association did not reach statistical significance. In this study, 26% of patients had no disease. Others have reported on the dissociation between anatomic markers of disease and standard risk factors.[11]

Among the 26 patients with a CCS of zero in our study, none were found to have obstructive disease, and only 1 (4%) was found to have noncalcified plaque. This finding is consistent with a report in which noncalcified plaques were the only manifestation of disease in 6% (10/161) of patients with a CCS of zero.[12] Because identification of noncalcified plaque may occur at an early stage of atherosclerosis that is more amenable to treatment, and plaque burden has been associated with vulnerable plaque, this subgroup of patients may benefit from early identification and early initiation of aggressive treatment to lower LDL. Whether the identification and characteristics of plaque as determined by CCTA add to the predictive value of the CCS is a promising, though unresolved, concept.[13] The relatively low yield of this finding raises issues as to the cost benefit and risk benefit in proceeding with CCTA after a CCS of zero in average patients, especially those without multiple risk factors.

Analysis of cholesterol management in this practice showed that patients who received a CCTA diagnosis of new disease, patients with an anatomic definition of existing disease with CCTA, and subgroups with plaque and hyperlipidemia all received more aggressive lipid control as a result of CCTA—despite near-normal LDL values at baseline—presumably as a result of cardiac anatomic imaging. The greatest reduction occurred in those groups with the greatest risk: patients with plaque (noncalcified and mixed) and patients with hyperlipidemia. This finding suggested that physicians targeted these patients selectively as a result of the CCTA findings, raising the issue of whether CCTA integrated into a cardiology practice offers more tailored cholesterol management than the CSS alone (except as noted above when the CCS is zero). Figure 2 shows a CCTA image and Figure 3 shows the LDL history of a patient with substantial plaque burden with near-significant occlusion. When this patient first presented in 2001, his LDL was 183 mg/dL. After the CCTA was obtained in 2006, the patient's lipid management was intensified.

This study showed a reduction in nuclear testing by 15% and a reduction in treadmill stress testing in excess of 40% early in the CCTA experience. We believe that a substantially greater reduction in multimodality testing is possible and even justified. The 26% of patients who had no disease would not require functional testing, in addition to many of the patients with new nonobstructive disease and many of the patients with existing disease. Accordingly, it would therefore not be surprising to expect a reduction in excess of 50% or more in myocardial perfusion imaging when CCTA is

Table 3
Comparison of Pre- and Post-CCTA Lipid Levels, by Patient Type

Characteristic	Normal (n = 10)	New CAD (n = 22)	Existing CAD (n = 26)	Soft Plaque Subset* (n = 15)	Hyperlipidemic Subset (Cholesterol > 200)† (n = 11)	Hyperlipidemic Subset (LDL > 130‡ (n = 9)
Total Cholesterol, Mean						
Pre-CCTA (mg/dL)	166.8	173.32	167.69	180.93	229.55	228.78
Post-CCTA (mg/dL)	167.8	159.27	141.96	159.87	167.64	167.89
Change (%)	0.6	−8.11	−15.34	−11.64	−26.97	−26.62
P Value	NS	NS (*P* = .056)	**.001**	NS (*P* = .054)	**.00005**	**.003**
LDL Cholesterol, Mean						
Pre-CCTA (mg/dL)	105.23	112.13	90.87	118.75	139.87	152.39
Post-CCTA (mg/dL)	104.2	95.64	78.42	95.6	99.91	103.89
Change (%)	−0.98	−14.71	−12.68	−19.49	−28.57	−31.83
P Value	NS	**.007**	**.037**	**.011**	**.006**	**.004**
HDL Cholesterol, Mean						
Pre-CCTA (mg/dL)	47.8	48	47.96	47.8	52.45	57.44
Post-CCTA (mg/dL)	44.4	48.73	44.65	46.13	41.82	44.22
Change (%)	−7.11	1.52	−6.9	−3.49	−20.27	−23.02
P Value	**.008**	NS	NS (*P* = .065)	NS	.017	.013

*Includes 12 new CAD patients, 2 existing CAD patients, and 1 normal patient.
†Includes 5 new CAD patients, 5 existing CAD patients, and 1 normal patient with total cholesterol > 200 mg/dL.
‡Includes 5 new CAD patients, 3 existing CAD patients, and 1 normal patient with LDL > 130 mg/dL.
CCTA, cardiac computed tomographic angiography; CAD, coronary artery disease; LDL, low-density lipoprotein; NS, not significant; HDL, high-density lipoprotein.

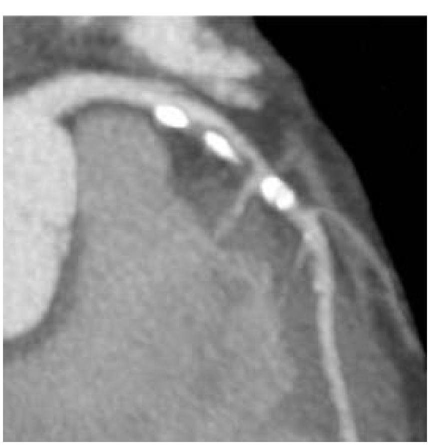

Figure 2. *A CCTA image in a 61-year-old man who presented with atypical chest pain and a history of treated hyperlipidemia, atypical chest pain, and a negative myocardial perfusion imaging study. His cardiac calcium score was 221 (60th percentile for his age). CCTA was obtained in 2006, and the study showed substantial plaque burden with near-significant occlusion. CCTA, cardiac computed tomographic angiography.*

used as the first diagnostic test in the intermediate-risk patient.

This study was not designed to evaluate the reduced number of invasive coronary angiography procedures, especially for those patients with equivocal or minor amounts of ischemia. This reduction was clearly observed in this practice, but it was not adequately quantified (and therefore not reported) due to variable adoption, variable interventional practice composition, and multiple laboratories used by the numerous group cardiologists. Furthermore, the impact of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial,[14] together with the reported late complications of stents,[15] may have already resulted in a national trend of reduced diagnostic cardiac catheterization and interventions, which has affected our ability to attribute the reductions in angiography and stent placement observed in this practice to CCTA alone. Nevertheless, the ability to offer CCTA instead of diagnostic catheterization provides an appealing alternative in the setting of higher standards for intervention and more widely adopted conservative medical approaches.

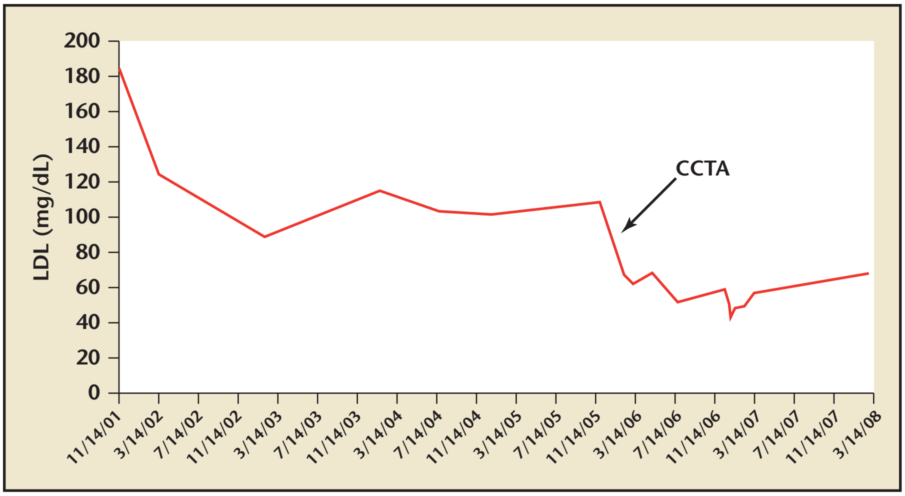

Figure 3. *LDL data for the same patient as shown in Figure 2. When the patient first presented in 2001, his LDL was 183 mg/dL. He was treated with statins to an LDL of 100 mg/dL. After CCTA in 2006 showed substantial plaque burden with near-significant occlusion, the patient's lipid management was intensified. His LDL level has been maintained below 70 mg/dL. CCTA, cardiac computed tomographic angiography; LDL, low-density lipoprotein.*

Although the CCS has been demonstrated to provide incremental and independent prognostic value over traditional risk factors, it has limitations. Left ventricular mass and ejection fraction, noncalcific plaque burden and assessment, and estimates of coronary stenosis can only be derived from contrast-enhanced studies. These variables are likely to have additional prognostic implications that may refine the predictive power of the CCS. The incremental prognostic value of adding CT angiography to CAC testing is promising but needs additional evaluation.[16]

Conclusions

With the advent of low-dose CCTA, which allows a substantial reduction in radiation exposure equal to CCS levels or 1-year of background radiation,[16-18] the role of CCTA as first-line testing for symptomatic and nonsymptomatic intermediate-risk patients deserves further study. Prospective evaluation should consider the effects of patient outcomes as measured by cholesterol management, diagnostic catheterization, intervention rates, and morbidity and mortality. ■

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Main Points

- The high specificity and negative predictive value of 64-slice coronary computed tomographic angiography (CCTA), combined with the ability to measure a calcium score for prognostic purposes and characterize plaque not seen with any other noninvasive technology, raises the likelihood that clinicians will use this technique in intermediate-risk patients.
- To assess the impact of CCTA on cardiology patients at a large urban primary and consultative cardiology practice, a retrospective analysis was performed based on 1-year follow-up of the first 100 patients evaluated onsite using 64-slice CCTA.
- In this study, a cardiac calcium score above 100 was associated with physician treatments that resulted in significant reduction in low-density lipoprotein in patients with normal low-density lipoprotein at baseline.
- Analysis of cholesterol management in this practice showed that patients who received a CCTA diagnosis of new disease, patients with an anatomic definition of existing disease with CCTA, and subgroups with plaque and hyperlipidemia all received more aggressive lipid control as a result of CCTA—despite near-normal LDL values at baseline—presumably as a result of cardiac anatomic imaging.
- This study showed a reduction in nuclear testing by 15% and a reduction in treadmill stress testing in excess of 40% early in the CCTA experience.

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