Diagnostic Performance of Computed Tomography Coronary Angiography (from the Prospective National Multicenter Multivendor EVASCAN Study)

Pascal Gueret, MD[a,*], Jean-François Deux, MD[b], Laurent Bonello, MD[c], Anthony Sarran, MD[d], Christophe Tron, MD[e], Luc Christiaens, MD[g], Jean-Nicolas Dacher, MD[f], David Bertrand, MD[f], Laurent Leborgne, MD[h], Cedric Renard, MD[i], Christophe Caussin, MD[j], Philippe Cluzel, MD[k], Gerard Helft, MD[l], Dominique Crochet, MD[m], Hélène Vernhet-Kovacsik, MD, PhD[n], Valérie Chabbert, MD[o], Emile Ferrari, MD[p], Martine Gilard, MD[q], Serge Willoteaux, MD[r], Alain Furber, MD[s], Gilles Barone-Rochette, MD[t], Adrien Jankowski, MD[u], Philippe Douek, MD[v], Elie Mousseaux, MD[w], Marc Sirol, MD[y], Ralph Niarra, MSc[x], Gilles Chatellier, MD[x], and Jean-Pierre Laissy, MD, PhD[z]

Computed tomographic coronary angiography (CTCA) has been proposed as a noninvasive test for significant coronary artery disease (CAD), but only limited data are available from prospective multicenter trials. The goal of this study was to establish the diagnostic accuracy of CTCA compared to coronary angiography (CA) in a large population of symptomatic patients with clinical indications for coronary imaging. This national, multicenter study was designed to prospectively evaluate stable patients able to undergo CTCA followed by conventional CA. Data from CTCA and CA were analyzed in a blinded fashion at central core laboratories. The main outcome was the evaluation of patient-, vessel-, and segment-based diagnostic performance of CTCA to detect or rule out significant CAD (≥50% luminal diameter reduction). Of 757 patients enrolled, 746 (mean age 61 ± 12 years, 71% men) were analyzed. They underwent CTCA followed by CA 1.7 ± 0.8 days later using a 64-detector scanner. The prevalence of significant CAD in native coronary vessels by CA was 54%. The rate of nonassessable segments by CTCA was 6%. In a patient-based analysis, sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios of CTCA were 91%, 50%, 68%, 83%, 1.82, and 0.18, respectively. The strongest predictors of false-negative results on CTCA were high estimated pretest probability of CAD (odds ratio [OR] 1.97, p <0.001), male gender (OR 1.5, p <0.002), diabetes (OR 1.5, p <0.0001), and age (OR 1.2, p <0.0001). In conclusion, in this large multicenter study, CTCA identified significant CAD with high sensitivity. However, in routine clinical practice, each patient should be individually evaluated, and the pretest probability of obstructive CAD should be taken into account when deciding which method, CTCA or CA, to use to diagnose its presence and severity. **(Am J Cardiol 2013;111:471−478)**

[a]Department of Cardiology and [b]Department of Radiology, Henri Mondor Hospital and University of Paris Est Créteil, Créteil, France; [c]Department of Cardiology and [d]Department of Radiology, North Hospital and Méditerranée University, Marseille, France; [e]Department of Cardiology and [f]Department of Radiology, Charles Nicolle Hospital and Rouen University, Rouen, France; [g]Department of Cardiology, University Hospital and Poitiers University, Poitiers, France; [h]Department of Cardiology and [i]Department of Radiology, South Hospital and Amiens University, Amiens, France; [j]Department of Cardiology, Marie Lannelongue Hospital, Le Plessis Robinson, France; [k]Department of Radiology and [l]Department of Cardiology, Pitié-Salpétrière Hospital and Paris VI University, Paris, France; [m]Department of Radiology, Laennec Hospital and Nantes University, Nantes, France; [n]Department of Radiology, Arnaud de Villeneuve Hospital and Montpellier University, Montpellier, France; [o]Department of Radiology, Rangueil Hospital and Toulouse University, Toulouse, France; [p]Department of Cardiology, Pasteur Hospital and Nice University, Nice, France; [q]Department of Cardiology, Cavale Blanche Hospital and Brest University, Brest, France; [r]Department of Radiology and [s]Department of Cardiology, University Hospital and Angers University, Angers, France; [t]Department of Cardiology and [u]Department of Radiology, Albert Michalon Hospital and Grenoble University, Grenoble, France; [v]Department of Radiology, Louis Pradel Hospital and Lyon 1 University, Lyon, France; [w]Department of Radiology and [x]Department of Biostatistics, Georges Pompidou European Hospital and Paris V University, Paris, France; [y]Department of Radiology, Lariboisière Hospital and Paris VII University, Paris, France; and [z]Department of Radiology, Bichat Hospital and Paris VII University, Paris, France. Manuscript received July 20, 2012; revised manuscript received and accepted October 17, 2012.

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*Corresponding author: Tel: +33-1-49-81-22-68; fax: +33-1-49-81-28-09.

E-mail address: pascal.gueret@hmn.aphp.fr (P. Gueret).

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Computed tomographic coronary angiography (CTCA) has been proposed as a noninvasive alternative to invasive coronary angiography (CA) for diagnosing obstructive coronary artery disease (CAD). Most published studies, the results of which have been reviewed in meta-analyses,[1,2] have been conducted in relatively limited numbers of patients by highly experienced investigators at single centers. These studies have found high negative predictive value (NPV) of CTCA. Although the diagnostic performance of 64-row computed tomography has now been assessed in a greater number of patients in multicenter trials,[3–7] their results suggest that a further large study reflecting "real-life" management may be useful to define the precise role of CTCA in patients with suspected CAD. The Evaluation of CT Scanner (EVASCAN) study is a large, national, multicenter, multivendor, prospective study in which data were analyzed at central core laboratories. Its main goal was to establish the diagnostic accuracy of 64-slice CTCA compared to conventional CA in a large population of symptomatic patients with clinical indications for anatomic coronary imaging.

Methods

The study was designed to prospectively evaluate stable adults with chest pain who were clinically referred for nonemergent invasive CA. Eligible patients were ≥18 years of age with known or suspected stable CAD, able to undergo CTCA and then CA within 4 days. The main exclusion criteria were unstable clinical status, serum creatinine >150 μmol/L, atrial fibrillation, pregnancy, and lactation. Patients were not excluded for elevated calcium score, heart rate, high body mass index, history of myocardial infarction, previous percutaneous coronary intervention, and/or coronary artery bypass grafting >6 months before CTCA.

The pretest probability of CAD was estimated using the Duke clinical score.[8] Patients were categorized as having low (1% to 30%), intermediate (31% to 70%), or high (71% to 99%) estimated pretest probability of significant CAD.

Protocols for patient enrollment, safety monitoring, image acquisition, and interpretation were developed by the EVASCAN steering committee. The institutional review board of Paris VI University approved the protocol, and all patients gave written informed consent.

All patients underwent 64-slice CTCA followed by conventional CA. The following systems were used: GE Healthcare (Milwaukee, Wisconsin) (69%), Philips Medical Systems (Andover, Massachusetts) (14%), Siemens Healthcare (Erlangen, Germany) (14%), and Toshiba Corporation (Tokyo, Japan) (3%). CTCA was performed using a standardized, optimized protocol for each system. All patients were in normal sinus rhythm before CTCA. A β blocker was recommended if heart rate was >65 beats/min. Patients first underwent an unenhanced prospective electrocardiographically gated acquisition for calcium scoring (Agatston score) and then a retrospective electrocardiographically gated contrast-enhanced acquisition to explore the coronary tree. The mean helical volume coverage in the z axis was 15 cm for the coronary tree. Typical parameters were a tube voltage of 100 to 120 kV for patients weighing <100 kg and 140 kV for the others, effective current intensity of 600 to 1,000 mA, slice collimation ranging from 0.5- to 0.75-mm slice thickness, and 0.35- to 0.5-second gantry rotation time, depending on the system used. Current intensity modulation was systematically applied to reduce radiation during systolic phases. The effective dose of the nonenhanced scan and CTCA was estimated from the dose-length product and a conversion coefficient (k = 0.014 mSv mGy cm) for the chest as the investigated anatomic region.[9]

A systematic reconstruction of the cardiac phases encompassing the RR interval (in 10% increments) was performed in all patients. Data were uploaded to dedicated workstations (Advantage Windows, GE Healthcare; Brilliance, Philips Medical Systems; Leonardo, Siemens Healthcare; and Vitrea, Toshiba Corporation).

Table 1
Baseline characteristics of the study population (n = 746)

Characteristic	Value
Age (yrs)	61 ± 12
Men	529 (71%)
Body mass index ≥30 kg/m^2	187 (25%)
Hypertension	388 (52%)
Diabetes mellitus	189 (25%)
Total cholesterol ≥220 mg/dl	150 (20%)
Smokers	191 (26%)
Family history of CAD	228 (31%)
Previous myocardial infarction	152 (20%)
Previous percutaneous coronary intervention	206 (28%)
Previous coronary bypass	32 (4%)
Chest pain at presentation	
Typical angina pectoris	418 (56%)
Atypical chest pain	234 (31%)
Suspected CAD	481 (65%)
Previously known CAD	259 (35%)
Creatinine (μmol/L)	88 ± 34
Heart rate during CTCA (beats/min)	63 ± 11
Agatston calcium score	396 ± 827

Data are expressed as mean ± SD or as number (percentage).

Table 2
Diagnostic performance of computed tomographic coronary angiography for the detection of ≥50% stenosis on coronary angiography in per patient, per vessel, and per segment analyses

Variable	Per Patient (n = 746)	Per Vessel (n = 2,969)	Per Segment (n = 10,767)
Stenoses by CA(*)	403 (54%)	790 (27%)	1,125 (10%)
Stenoses by CTCA	539	963	1,604
False-positives	172	410	1,098
False-negatives	36	237	619
Sensitivity (95% CI)	91% (88–93)	70% (67–73)	45 (42–48)
Specificity (95% CI)	50% (45–55)	81% (79–83)	88 (88–89)
PPV (95% CI)	68% (64–72)	57% (54–61)	32 (29–34)
NPV (95% CI)	83% (77–89)	88% (87–90)	93 (93–94)
Positive likelihood ratio (95% CI)	1.82 (1.63–2.03)	3.72 (3.37–4.11)	3.95 (3.63–4.30)
Negative likelihood ratio (95% CI)	0.18 (0.13–0.25)	0.37 (0.33–0.41)	0.62 (0.59–0.65)

* Prevalence of CAD.

Table 3
Diagnostic performance of computed tomographic coronary angiography for the detection of ≥50% stenosis on coronary angiography in the per patient analysis

Variable	n	CAD Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Overall	746	54%	91% (88%−93%)	50% (45%−55%)	68% (64%−72%)	83% (77%−89%)	1.82 (1.63−2.03)	0.18 (0.13−0.25)
By gender								
Male	529	61%	91% (88%−94%)	47% (40%−53%)	73% (69%−77%)	77% (70%−85%)	1.71 (1.50−1.95)	0.19 (0.13−0.27)
Female	217	36%	90% (83%−96%)	55% (46%−63%)	53% (44%−61%)	92% (84%−97%)	1.98 (1.63−2.41)	0.19 (0.10−0.37)
Chi-square			0.21	2.17	18.84	5.75	37.87	
p value			0.65	0.14	<0.001	0.016	<0.001	
By heart rate (beats/min)								
<65	458	53%	90% (86%−94%)	49% (42%−56%)	67% (62%−72%)	82% (75%−88%)	1.78 (1.55−2.04)	0.20 (0.13−0.30)
≥65	288	56%	93% (88%−97%)	51% (42%−59%)	70% (63%−76%)	84% (76%−93%)	1.88 (1.57−2.25)	0.15 (0.08−0.26)
Chi-square			0.67	0.07	0.67	0.28	15.23	
p value			0.04	0.79	0.41	0.60	<0.001	
By body mass index (kg/m^2)								
<25	221	53%	88% (82%−93%)	57% (46%−65%)	69% (62%−77%)	81% (71%−90%)	1.99 (1.59−2.49)	0.21 (0.13−0.36)
25−30	318	56%	92% (88%−86%)	49% (41%−57%)	69% (63%−75%)	83% (75%−91%)	1.80 (1.53−2.13)	0.17 (0.08−0.34)
≥30	187	45%	92% (87%−97%)	46% (36%−57%)	68% (60%−76%)	83% (72%−94%)	1.72 (1.40−2.12)	0.17 (0.08−0.34)
Chi-square (trend)			1.64	1.82	0.05	0.14	39.68	
p value			0.20	0.18	0.82	0.71	<0.001	
Diabetes mellitus								
No	557	53%	91% (87%−94%)	49% (43%−55%)	67% (62%−72%)	84% (76%−88%)	1.79 (1.58−2.03)	0.19 (0.13−0.28)
Yes	189	57%	93% (86%−97%)	49% (40%−62%)	71% (63%−79%)	84% (71%−93%)	1.90 (1.51−2.238)	0.15 (0.07−0.29)
Chi-square			0.38	0.08	0.85	0.09	15.43	
p value			0.78	0.78	0.36	0.77	<0.001	
By risk level*								
Low	102	21%	86% (77%−100%)	49% (38%−60%)	31% (19%−42%)	93% (85%−100%)	1.69 (1.28−2.23)	0.29 (0.11−0.84)
Intermediate	201	44%	87% (79%−99%)	55% (46%−56%)	61% (52%−69%)	84% (75%−92%)	1.94 (1.55−2.42)	0.264 (0.14−0.42)
High	402	69%	92% (89%−96%)	45% (36%−54%)	79% (74%−83%)	73% (63%−83%)	1.67 (1.42−1.97)	0.17 (0.11−0.27)
Chi-square (trend)			0.35	0.02	51.65	7.49	15.43	
p value			0.55	0.91	<0.001	0.006	<0.001	
By calcium score								
0	147	21%	81% (67%−95%)	61% (52%−71%)	36% (24%−47%)	92% (86%−98%)	2.08 (1.56−2.77)	0.32 (0.15−0.66)
1−100	110	45%	82% (71%−93%)	56% (43%−68%)	60% (48%−71%)	79% (67%−91%)	1.84 (1.35−2.52)	0.33 (0.18−0.62)
100−600	70	63%	93% (86%−100%)	50% (31%−69%)	76% (65%−87%)	81% (62%−100%)	1.86 (1.26−2.76)	0.14 (0.04−0.43)
≥600	79	81%	93% (93%−100%)	27% (4%−49%)	85% (77%−94%)	67% (29%−100%)	1.32 (0.97−1.80)	0.12 (0.02−0.58)
Chi-square (trend)			4.25	4.17	15.08	1.36	48.79	
p value			0.04	0.04	<0.0001	0.24	<0.001	

* Low, 1% to 30%; intermediate, 31% to 70%; high, 71% to 100%.

Table 4
Univariate and multivariate logistic regression analysis: parameters independently associated with false-negative results and with nonassessable coronary segments on computed tomography coronary angiography

Variable	Univariate Analysis			Multivariate Analysis		
	OR	(95% CI)	p Value	OR	(95% CI)	p Value
False-negative results						
Age	1.2	(1.1−1.3)	<0.0001	1.2	(1.1−1.3)	<0.001
Gender (male vs female)	2.0	(1.6−2.4)	<0.0001	1.5	(1.16−1.94)	0.0023
Diabetes (yes vs no)	1.6	(1.3−1.9)	<0.0001	1.5	(1.26−1.82)	<0.0001
Body mass index (≥30 vs <30 kg/m^2)	1.0	(0.9−1.3)	0.66	1.0	(0.80−1.19)	0.8407
Heart rate (≥65 vs <65 beats/min)	1.1	(0.9−1.3)	0.49	1.1	(0.92−1.31)	0.3058
Pretest probability groups						
Intermediate vs low	1.4	(0.9−2.0)	0.10	1.1	(0.69−1.66)	0.8697
High vs low	3.2	(2.3−4.4)	<0.0001	1.9	(1.28−3.05)	0.0013
Nonassessable coronary segments						
Age	1.00	(0.99−1.01)	0.96	1.0	(0.98−1.01)	0.67
Gender (male vs female)	1.38	(1.17−1.62)	<0.0001	1.14	(0.85−1.5)	0.39
Diabetes (yes vs no)	1.30	(1.10−1.54)	<0.002	1.04	(0.76−1.42)	0.82
Artifact (yes vs no)	2.72	(2.32−3.20)	<0.001	2.53	(1.88−3.41)	<0.001
Body mass index (≥30 vs <30 kg/m^2)	1.92	(1.63−2.25)	<0.001	2.72	(2.07−3.66)	<0.001
Heart rate (≥65 vs <65 beats/min)	2.06	(1.77−2.41)	<0.001	1.43	(1.08−1.89)	0.01
Segment diameter (<1.5 vs ≥1.5 mm)	19.26	(16.13−23.00)	<0.001	18.66	(13.93−24.97)	<0.001
Calcium score (≥600 vs <600)	1.61	(1.24−2.08)	0.0003	1.74	(1.23−2.47)	<0.002
Segment (distal vs proximal/medial)	2.70	(2.29−2.32)	<0.001	1.98	(1.46−2.68)	<0.001
Location of stenosis (in circumflex coronary artery vs left anterior descending coronary artery or right coronary artery)	2.09	(1.79−2.44)	<0.001	1.64	(1.24−2.16)	0.0005

Conventional CA was performed using standard techniques with a transfemoral or transradial approach.[10] All studies were performed using digital equipment. Multiple projections were obtained as deemed necessary by the angiographer.

The results of CTCA and CA were analyzed visually in separate central core laboratories in a blinded manner by experienced readers who were unaware of patients' clinical information or the results of the alternative imaging technique.

Coronary arteries were scored using the coronary artery classification of the American Heart Association.[11] Each coronary segment was visually graded as individually assessable or not, normal, nonsignificant stenosis (<50%), stenosis ≥50%, or total occlusion. In case of multiple lesions in a given segment or artery, the worst lesion was considered. Importantly, nonassessable segments by CTCA were counted as positive for stenosis (≥50%).[12]

Using a binary end point for each patient (agreement between CTCA and CA), expecting a 50% to 65% prevalence of CAD, sensitivity of 0.85, specificity of 0.9, accuracy of 4%, and a 10% dropout rate, it was considered necessary to enroll 650 to 875 patients.

Measures of diagnostic accuracy of CTCA for the detection of significant CAD on native coronary vessels (sensitivity, specificity, positive predictive value [PPV], and NPV, with their corresponding 95% confidence intervals [CIs], as well as positive and negative likelihood ratios of CTCA) were calculated on per-patient, per-vessel, and per-segment bases.

Results are expressed as point estimates and their exact 95% CIs, while continuous variables are presented as mean ± SD when normally distributed. All statistical tests were 2 sided. Chi-square tests were used to compare categorical variables. Analysis of variance or nonparametric Kruskal-Wallis tests were used to compare continuous variables depending on their normality. Interobserver reproducibility for the detection of significant CAD stenosis (<50% vs ≥50%) in computed tomographic coronary angiographic images was evaluated by κ statistics between 2 observers unaware of the results of CA who analyzed the computed tomographic scans of 30 patients randomly selected. The κ statistic was 0.58 (95% CI 0.28 to 0.88). Multivariate stepwise logistic regression analysis was used to calculate the odds ratios (ORs) and 95% CIs and to identify the independent predictors of false-negative results on CTCA as well as of nonevaluable coronary segments by CTCA. To compare the likelihood ratios between subgroups, the logistic regression models of the prior odds and posterior odds were used.[13] Analyses were carried out using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

Results

Between June 2006 and June 2008, 40 centers prospectively enrolled 757 patients; data from 746 were analyzed. Of the 11 patients excluded from the analysis, 8 had incomplete or canceled CTCA or CA, 2 had protocol deviations, and 1 withdrew consent.

Demographic and clinical characteristics are listed in Table 1. The mean age was 61 ± 12 years, 71% were men, and most patients had not previously been diagnosed with CAD (n = 481 [65%]). The main cardiovascular risk factors were hypertension in 52% of patients, smoking in 26%,

Table 5
Diagnostic performance of computed tomographic coronary angiography for the detection of ≥50% stenosis on coronary angiography in per vessel and per segment analyses

Variable	n	CAD Prevalence	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Overall vessel	2,669	27%	70% (67%–73%)	81% (78%–83%)	57% (54%–61%)	88% (87%–90%)	3.72 (3.37–4.11)	0.37 (0.33–0.41)
By vessel type								
Right coronary artery	2,669	32%	74% (71%–76%)	78% (77%–80%)	61% (59%–64%)	86% (85%–88%)	3.41 (3.11–3.74)	0.34 (0.30–0.37)
Left anterior descending coronary artery	2,669	40%	77% (75%–80%)	70% (67%–72%)	63% (61%–66%)	82% (80%–84%)	2.53 (2.34–2.73)	0.33 (0.29–0.37)
Circumflex coronary artery	2,669	30%	61% (58%–64%)	73% (71%–74%)	49% (46%–52%)	81% (79%–83%)	2.22 (2.04–2.42)	0.54 (0.49–0.59)
Chi-square			139.44	17.79	35.33	232.06	213.45	
p value			<0.001	<0.001	<0.001	<0.001	<0.001	
Overall segments	1,0767	10%	45% (42%–48%)	88% (88%–89%)	32% (29%–34%)	93% (93%–94%)	3.95 (3.63–4.30)	0.62 (0.59–0.65)
By vessel diameter (mm)								
<1.5	895	12%	65% (56%–74%)	62% (59%–66%)	19% (15%–23%)	93% (90%–95%)	1.73 (1.47–2.04)	0.56 (0.43–0.73)
≥1.5	9,818	10%	43% (40%–46%)	91% (91%–92%)	35% (34%–39%)	93% (93%–94%)	4.9 (4.52–5.51)	0.63 (0.59–0.66)
Chi-square			19.12	511.64	37.87	0.06	99.19	
p value			<0.001	<0.001	<0.001	0.81	<0.001	
By segment location								
Distal	5,024	9%	33% (29%–37%)	88% (87%–89%)	22% (19%–25%)	93% (92%–94%)	2.79 (2.40–3.25)	0.76 (0.71–0.81)
Proximal/medial	5,743	12%	53% (49%–57%)	89% (88%–90%)	39% (36%–42%)	94% (93%–94%)	4.83 (4.35–5.37)	0.53 (0.48–0.57)
Chi-square			44.23	1.49	51.19	1.40	186.82	
p value			<0.001	0.22	<0.001	0.24	<0.001	

body mass index ≥30 kg/m^2 in 25%, diabetes in 25%, and hypercholesterolemia in 20%.

CA was performed 1.7 ± 0.8 days after CTCA. The estimated radiation dose for CTCA was 17.2 ± 5.9 mSv. The mean heart rate during CTCA was 63 ± 11 beats/min. Additional β blockers were administered before scanning in 20% of patients. The mean Agatston calcium score was 396 ± 827, and 11% of patients had calcium scores ≥600.

From the coronary angiographic analysis, the prevalence of ≥1 coronary lesion ≥50% was 54% (403 patients). Among these, 41% had single-vessel disease, 34% had 2-vessel disease, 23% had 3-vessel disease, and 2% had significant coronary lesions in the left main coronary artery.

Most patients with significant coronary stenosis on CA were identified by CTCA (367 of 403, a 91% true-positive rate). In 114 of 125 patients (91%) with left main or 3-vessel disease, CTCA detected ≥1 significant lesion. Thirty-six patients with CAD were missed by CTCA (a 9% false-negative rate). CTCA correctly ruled out significant CAD in 171 of 343 patients without significant stenosis using CA (a true-negative rate of 50%). (Tables 2 and 3) However, because nonassessable segments were considered as stenosed, the false-positive rate was 50%. If nonassessable segments were assumed to be negative for coronary stenosis, sensitivity would decrease (from 91% to 84%), as would NPV (from 83% to 80%), but specificity would increase (from 50% to 74%), as would PPV (from 68% to 79%).

Our results show that coronary arterial calcification (calcium score) significantly alters the diagnostic performance of CTCA. There was a statistically significant trend toward increased sensitivity ($p < 0.04$) and PPV ($p < 0.0001$) and decreased specificity ($p < 0.04$) with increased calcium score (Table 3). Interestingly, the absence of coronary calcium alone was not sufficient to exclude CAD (21% CAD prevalence in 147 patients with calcium scores of 0). In such patients, CTCA was highly effective to rule out significant CAD (NPV 92%).

The analysis comprised 102 patients (14%) with low, 201 (28%) with intermediate, and 402 (57%) with high estimated pretest probability for CAD (incomplete data in 41 patients). No significant differences were noted in sensitivity and specificity. However, as expected, PPV increased with risk level, and in contrast, NPV was higher in patients with low pretest likelihood of CAD (Table 3).

Among false results of CTCA, false-negative results may be detrimental to patient management, because clinicians may be reassured about patients' coronary artery anatomy. We performed a logistic regression analysis to identify clinical parameters predictive of false-negative results (Table 4). On multivariate analysis, factors that increased the likelihood of false-negative results on CTCA were age (OR 1.2, $p < 0.001$), male gender (OR 1.5, $p < 0.002$), diabetes (OR 1.5, $p < 0.0001$), and high estimated pretest probability of CAD (OR 1.9, $p < 0.001$).

Overall disease prevalence was 27% of vessels (Tables 2 and 5). Most vessels with significant coronary stenosis on CA were identified by CTCA (553 of 790, a 70% true-positive rate), whereas 237 vessels with CAD were missed by CTCA (a 30% false-negative rate). CTCA overestimated the extent of disease in 410 of 2,179 vessels (a 19%

false-positive rate) and correctly ruled out significant CAD in 1,769 of 2,179 vessels without significant stenosis using CA (an 81% true-negative rate). Overall, the diagnostic performance of CTCA was slightly better for the left anterior descending coronary artery and right coronary artery than for the circumflex coronary artery (Table 5).

Overall, 10,767 segments were included for comparison with CA. All of these were evaluated, including segments with calcifications and those <1.5 mm in diameter. Overall disease prevalence was 10% of segments by CA (Tables 2 and 5). The severity of 619 coronary stenoses was underestimated and classified as nonsignificant or normal by CTCA (a 55% false-negative rate), whereas the severity of 1,098 nonsignificant lesions was overestimated by CTCA (an 11% false-positive rate). Sensitivity was lower but specificity and PPV were higher in segments ≥1.5 mm in diameter ($p < 0.001$).

A total of 687 segments (6%) were judged as nonassessable by CTCA. For statistical analysis, these segments were considered as stenosed. However, 533 of them (78%) were normal or had nonsignificant lesions by CA. The prevalence of nonassessable segments was 23% in the left anterior descending coronary artery, 46% in the circumflex coronary artery, and 30% in the right coronary artery. Nonassessable segments were more often located in distal segments (69%) than in proximal or medial segments (31%) ($p < 0.001$). Univariate regression analysis identified 9 variables associated with nonassessable coronary segments by CTCA as judged by readers (Table 4). Multivariate logistic regression analysis showed that vessel size <1.5 mm, obesity (body mass index ≥30 kg/m^2), artifacts (motion, respiratory, and heart rhythm irregularity), distal location of stenoses in coronary segments, presence of calcifications (Agatston score ≥600), and location of stenosis in the circumflex coronary artery were independently associated with nonassessable coronary segments by readers.

Discussion

The diagnostic value of CTCA was first studied extensively using 16-detector systems and more recently with 64-slice computed tomographic scanners that benefit from better temporal resolution and acceptable spatial resolution. The high NPVs reported by many investigators have led to the proposal of CTCA as the method of choice to exclude significant coronary stenosis, particularly in patients without histories of CAD. Therefore, on the basis of these reports, expert consensus[14] and appropriate use criteria[15] documents have recently been published.

In this prospective, multicenter, multivendor study, which included the largest number of intermediate- to high-risk stable and symptomatic patients reported to date, CTCA had reliable accuracy to detect or correctly rule out significant CAD. In this population of patients (CAD prevalence in native coronary vessels 54%), sensitivity was 91% and NPV was 83%. Because of a trend toward overestimation of the severity of stenosis, specificity was only 50% and PPV was 68%. The main reasons were the inclusion of all segments in our analysis and the decision to consider nonassessable segments as stenosed.

Comparison of the EVASCAN study results to those of other multicenter trials is made difficult by heterogeneity with respect to the patient populations. In some studies, all patients had suspected CAD,[4,5] whereas in others, there was a mix of suspected and known CAD.[3,6,7] The actual prevalence of CAD ranged from 25%[5] to 68%.[4] Also, patients with histories of percutaneous coronary intervention or coronary artery bypass graft surgery were excluded in these trials[3–7] but not in the EVASCAN study. In 1 study,[3] patients were excluded for an elevated calcium score, which was not the case in other studies.[4,5] Finally, unlike the Coronary Artery Evaluation Using 64-Row Multidetector CT Angiography (CORE 64) trial,[3] we did not exclude segments <1.5 mm in diameter from analysis. In the CORE 64 trial, which included 291 patients, the reported NPV was 83% in a patient-based analysis (compared to >95% in previous single-center studies),[1,2] although patients with calcium scores >600 and segments <1.5 mm in diameter were excluded from the analysis.[3]

Bearing in mind that relevant coronary segments are essentially those suitable for revascularization (diameter ≥1.5 mm), our results suggest that CTCA cannot replace conventional CA at present. However, this should not attenuate the prognostic usefulness of CTCA claimed by some investigators who have reported a lack of adverse cardiac events during short-term follow-up in patients with normal results on CTCA.[16,17]

Exact correspondence between CTCA and CA for classifying coronary stenosis severity cannot be expected. The current spatial resolution of CTCA may not be adequate for accurately determining anatomic severity, which is quite often overestimated. Moreover, coronary angiographic analysis was qualitative rather than quantitative. Interestingly, Meijboom et al[4] pointed out that the highest frequency of overestimated (false-positive) and underestimated (false-negative) coronary stenosis by CTCA was clustered around the cutoff value of 50% diameter reduction as determined by quantitative CA.

Similarly to Meijboom et al,[4] but contrary to other studies,[18–23] we did not exclude nonevaluable coronary segments from analysis, instead assigning them as stenosed. This may have significant effects on the diagnostic performance of the technique, as shown by Shapiro et al.[12] Scoring all nonassessable segments as stenosed maximizes the sensitivity and NPV at the cost of decreased specificity and PPV. However, this approach is more appropriate from a clinical standpoint, because in an intention-to-treat approach, patients with either positive results on CTCA or nonassessable segments will undergo further CA.[4] Our multivariate analysis identified several independent parameters associated with nonevaluable segments. Diagnostic accuracy appears limited for the identification of stenoses located in distal vessels and/or those <1.5 mm in diameter, which tended to be distal and would not be proposed for revascularization. However, the identification of significant CAD remains mandatory to manage these patients and to alleviate their symptoms with medical treatment.

A limitation of this study was the qualitative and subjective assessment of coronary stenosis used with the 2 techniques. Quantitative CA is used mainly for clinical research, whereas at most centers, diagnosis and severity of

CAD are routinely established qualitatively by means of a crude visual estimation of the degree of luminal diameter stenosis. In a study comparing conventional CA with 64-slice CTCA, the diagnostic yield was higher when qualitative analysis was performed.[21]

Radiation exposure can be a limitation of CTCA. The estimated effective radiation dose in the present study was high (17.2 ± 5.9 mSv), but it is in line with previous multicenter reports[3,4,7] and reflects the real-world clinical practice at the time the patients were included. Recent technical modalities proposed by manufacturers for reducing radiation exposure were not available in most of the computed tomographic coronary angiographic scanners used in the study. However, our results concur with the observations reported in the International Prospective Multicenter Study on Radiation Dose Estimates of Coronary CT Angiography in Daily Practice (PROTECTION I) trial,[24] in which 120 sites reported an average radiation dose of 12 mSv, with large variations ranging from 4 mSv to nearly 30 mSv. The diagnostic performance of CTCA obtained in this large cohort of unselected, stable, symptomatic patients may aid in the development of guidelines for the application of CTCA in this population.[25–27] From a practical point of view, among other clinical characteristics, pretest probability for significant CAD is an important parameter to consider to identify patients in whom CTCA is most effective in detecting significant coronary stenosis.

Disclosures

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Supplementary data

Supplementary data containing the list of individuals to whom the authors would like to acknowledge for their contributions to this project can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2012.10.029.

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