Ontario Multi-detector Computed Tomographic Coronary Angiography Study (OMCAS):

An Evaluation of Diagnostic Accuracy

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Abstract

Background: Following the acquisition of new 64 slice multidetector computed tomographic (MDCT) units in Ontario, the Ontario Health Technology Advisory Committee, based on a review of the literature, recommended that a field evaluation be conducted to examine the use of computed tomographic coronary angiography. The Ontario Multidetector Computed Tomography Coronary Angiography Study (OMCAS) was designed as a multicentre, non-randomized, single blinded study to evaluate 64-slice MDCT coronary angiography and conducted at 4 academic teaching hospitals in the province.

Methods: Enrolled in the study were patients scheduled for a conventional invasive coronary angiogram (ICA) whom also agreed to receive an additional non-invasive coronary angiography using 64-slice multidetector computed tomography (CTA). Two patient groups were evaluated: those individuals with valvular heart disease, cardiomyopathy or congenital heart disease undergoing CICA for diagnosis of coronary artery disease (CAD) prior to surgical intervention and secondly individuals with an intermediate probability of CAD. Images for both CTA and ICA were assessed independently by two reviewers from the same centre. A 3rd consensus review was conducted when differences in the degree of stenosis at both the patient and vessel level. Comparative analysis between ICA and CTA was completed using a categorical analysis as follows: normal, < 50% stenosis, 50-69% stenosis, 70-99% stenosis and occluded or unevaluable.

Results: Enrolment in the study between September 2006 to June 2009 resulted in 181 patients being recruited with data available for 169 individuals with both CTA and ICA results. For all patients diagnostic accuracy for CTA relative to ICA was for the sensitivity and specificity 81.3% (95%CI 71.0%,89.1%) and 93.3%, (95%CI 85.9%,97.5%) respectively at the 50% stenosis level. At a 70% stenosis level, for all patients the diagnostic accuracy for CTA relative to ICA was 75.7% (95%CI 64.0%,85.2%) and 93.9%, (95%CI 87.3%,97.7%) for the sensitivity and specificity respectively. Radiation exposure from CTA was 61% greater than with ICA (P<0.001). Between centre differences with respect to diagnostic operating characteristics were observed.

Discussion: The diagnostic operating characteristics of CTA observed in this study were characterized by a lower sensitivity than previously published. The utilization of CTA should be accompanied by the establishment of acquisition protocols, patient criteria for which the diagnostic test is most suited and the understanding of downstream resource utilization and implications related to the use of other diagnostic modalities used for CAD. It is also important to recognize that the results of a single centre may not necessarily be generalizable to all centres.

Table of Contents

Abbreviations

AUC	area under curve
CAD	coronary artery disease
CTA	computed tomographic coronary angiography
ECG	electrocardiogram
FN	false negative
FP	false positive
ICA	invasive coronary angiography
MAS	Medical Advisory Secretariat
MDCT	multidetector computed tomography
MOHLTC	Ontario Ministry of Health and Long-Term Care
NPV	negative predictive value
OHTAC	Ontario Health Technology Advisory Committee
OMCAS	Ontario multi-detector computed tomographic coronary angiography study
OR	odds ratio
PATH	Program for Assessment of Technology in Health Research Institute
PPV	positive predictive value
ROC	receiver operating characteristic
TN	true negative
TP	true positive
VD	vessel disease

List of Tables

List of Figures

Background

Coronary artery disease (CAD) affects approximately 1.3 million Canadians on a yearly basis and is the second leading cause of death in Canada.[1,2] Although the prevalence of CAD appears to be on a decline nationwide[1], current trends suggest that it may increase in the coming years due to growing high risk populations[3].

Coronary artery disease is caused by a build up of plaque within the arteries referred to as atherosclerosis.[4] A continual build up of plaque can lead to obstruction within the vessel causing acute myocardial infarction, stroke or other acute cardiovascular events. The gold standard intervention for identifying CAD is conventional invasive coronary angiography (ICA). In this procedure, a contrast medium is injected into the coronary arteries of patients suspected of having CAD. X-rays images can then be captured on video screen and viewed as images or motion pictures enabled by the contrast medium[5,6,7]. However, ICA may put the patient at risk of further complications including stroke, cerebral ischemia or neurological complications, coronary artery complications, and even death.[7] Patients are also exposed to radiation[5,6,7] and the cost of the procedure is significant.[8,9]

Multi-detector computed tomography coronary angiography (CTA) is a non-invasive technique that is increasingly being used within CAD diagnostic regimens. It involves inserting a contrast dye into the peripheral vein of the patient who is then positioned onto a CT scanner. A series of X-rays images, often referred to as ‘slices’, are taken from varying angles in order to reconstruct a 3-dimenstional image of the heart’s anatomy. The 64-slice MDCT was introduced in 2004[5] and is preferred to its

predecessors (32-slice and 16 slice CTA) due to improvements in image quality and temporal resolution.[6] The Ontario Ministry of Health and Long-term Care (MOHLTC) faced with the need to replace aging CT machines announced funding in 2004 for the acquisition of 27 new 64-slice MDCT scanners to be distributed across the province in 2005.[10,11] At the time of the introduction into the health system of the 64-slice MDCT scanners in 2005, Ontario patients undergoing an elective cardiac catheterization in Ontario were waiting for a median of 15 days ranging from 3 days to 63 days for elective catheterization procedures depending on the institution, with over 1,700 people waiting for a cardiac catheterization in the province.[12] The utilization of 64-slice CTA in the Province of Ontario was also thought to potentially reduce the demand for elective ICA.

In 2005, a systematic review of the CTA literature was conducted by the MOHLTC Medical Advisory Secretariat (MAS).[11] This review identified 13 studies that compared the diagnostic accuracy of 16-slice CTA to conventional coronary angiography and concluded that 16-slice CTA may not be accurate enough to detect and rule out CAD. Published studies describing the diagnostic accuracy of 64-slice CTA for CAD were also searched for as a part of this review. However, no published studies examining the use of this newer technology for this indication were identified.[11]

The Ontario Health Technology Advisory Committee (OHTAC), upon review of the report by the MAS, determined, based on the evidence presented, that the utility of both 16-slice and 64-slice CTA was still uncertain and recommended that *"a field evaluation to determine the effectiveness, clinical utility and cost-effectiveness of 64-slice CT to diagnose CAD be undertaken."*[10,11]

The Ontario Multi-detector Computed Tomographic Coronary Angiography Study (OMCAS) was therefore designed to provide OHTAC with province specific information regarding the use of 64-slice CTA and to help inform health policy decision making. This multicentre study was conducted at 4 academic teaching centres across the province and was a collaborative effort by the Programs for Assessment of Technology in Health (PATH) Research Institute and the participating academic teaching hospitals with representation, consisting of at least 1 radiologist and 1 cardiologist, from each centre.

This multi-center, non-randomized, single blinded study evaluated the effectiveness and clinical utility of 64-slice CTA in the investigation of coronary artery disease in patients as compared to ICA. The objectives of the study were as follows:

1. To determine the sensitivity and specificity of 64-slice CTA for detecting coronary artery disease as defined by ICA.
2. To assess the effectiveness of 64-slice CTA to eliminate the need of ICA and cardiac catheterization in patients with valvular heart disease, congenital heart disease, or cardiomyopathy.
3. To evaluate the clinical utility of 64-slice CTA in symptomatic patients with an intermediate probability of coronary artery disease who are scheduled for ICA.
4. To establish acquisition and analysis protocols for the conduct of 64-slice.

Methods

Study setting and patient population

Patients already booked for invasive cardiac catheterization at one of four university teaching hospitals (St. Michael's Hospital (SMH), Sunnybrook Health Sciences Centre (SB), University Health Network (UHN) and the University of Ottawa Heart Institute (UOHI)) in Ontario were enrolled in the study between September 2006 and June 2009. Two patient groups requiring ICA were evaluated in this study: 1) patients with a lower probability of CAD including patients with valvular heart disease, congenital heart disease or cardiomyopathy; and 2) patients with an intermediate probability of CAD. Excluded from the study were patients less than 18 years of age, with a high pre-test probability (> 90%) for CAD or documented CAD with a history of revascularization, renal insufficiency (glomerular filtration rate < 40 mL/min for non-diabetics and < 60 mL/min for patients with diabetes mellitus), a contrast agent allergy, pregnancy or breastfeeding, an uncontrolled heart rate, chronic atrial fibrillation and those unable to perform a 20 second breath-hold. Each eligible patient consenting to participate in the study received prior to their scheduled ICA, with no intervening cardiac event, an additional diagnostic coronary angiographic evaluation with a 64-slice MDCT. In all cases the CTA was performed within 10 working days prior to ICA.

Data collection and patient characterization

Demographic information (e.g. age, height, and weight), factors present pre-CTA (e.g. chest pain syndrome), risk factors/medical history (e.g. hypertension), symptoms (e.g. description of pain), electrocardiogram (ECG) results, previous non-invasive test results

(e.g. treadmill exercise test), current oral medications (e.g. beta-blockers) were obtained for each patient participating in the study. After the traditional non-invasive testing modalities (exercise ECG, or stress myocardial perfusion imaging or echocardiography), the "pre-test probability" of CAD prior to CTA was calculated as suggested by Diamond and Forrester.[13,14]

CTA and ICA protocols

CTA image acquisition was performed according to enrolling centres clinical protocols. When necessary, metoprolol or diltiazem (oral and/or intravenous) was administered targeting a heart rate of ≤65 beats per minute and, nitroglycerin (0.3-0.8mg) was administered sublingually, if not contraindicated.

Retrospective ECG-gated data sets were acquired with either a GE Volume CT scanner (GE Healthcare, Milwaukee, Wisconsin) (SB, SMH and UOHI) or the Aquilion 64 MDCT scanner (Toshiba Medical Systems, Japan) (UHN). A tri-phasic intravenous contrast (Visipaque 320 or Omnipaque 350 (GE Healthcare, Princeton, New Jersey) administration protocol was used a bolus tracking or timing bolus technique. Contrast infusion rates adjusted according to patient weight and scan duration using a minimum of 4 mL/sec (< 60 kg), 5 mL/sec (60 and 80 kg), and 6 mL/sec (> 80 kg) for a total of 60-120 mL followed by a 50 mL saline bolus.

As per normal care, patients underwent ICA. Multiple oblique views were obtained to ascertain coronary anatomy. Choice of catheters, contrast and views were left to the discretion of the experienced coronary angiographer.

Image interpretation

Both the CTA and ICA images were each read by two blinded readers at each site and where discrepancies between readers were found a third consensus read of the image was completed. A 17 segment model of the coronary arteries and 4 point grading score (normal, mild (<50%), moderate (50-69%), severe (≥70%)) was used for the evaluation of coronary stenosis. "Unevaluable" segments were "forced" to classify all segments into one of the categories irrespective of image "quality". For CTA plaque was identified as soft, calcified or both. The determination of obstructive CAD was evaluated as coronary diameter stenosis ≥50% and ≥70%. Patient-level and vessel-level evaluation was completed. In patients with obstructive CAD further categorization of non-high risk or high risk CAD was completed (CAD-Model 1). In this model, high risk CAD was defined as having a left main stenosis (≥50%), or 3 vessel disease (VD) (≥70%) or 2-VD (≥70%) involving the proximal left anterior descending artery) [15,16]. Additionally, patients with obstructive CAD (≥50% diameter stenosis) were also categorized as 1-, 2-, or 3-vessel disease (CAD-Model 2)[17,18]

Statistical analyses

Statistical analyses were performed using SAS (version 9.1.3, SAS Institute Inc., Cary, North Carolina), and statistical significance was defined as P-value<0.05. Continuous variables with normal distributions were presented as means and standard deviations and those with non-normal distribution as median and interquartile ranges. Categorical variables were presented as frequencies with percentages for subject characteristics and CTA imaging parameters and a Wilcoxon rank sum test was used for continuous

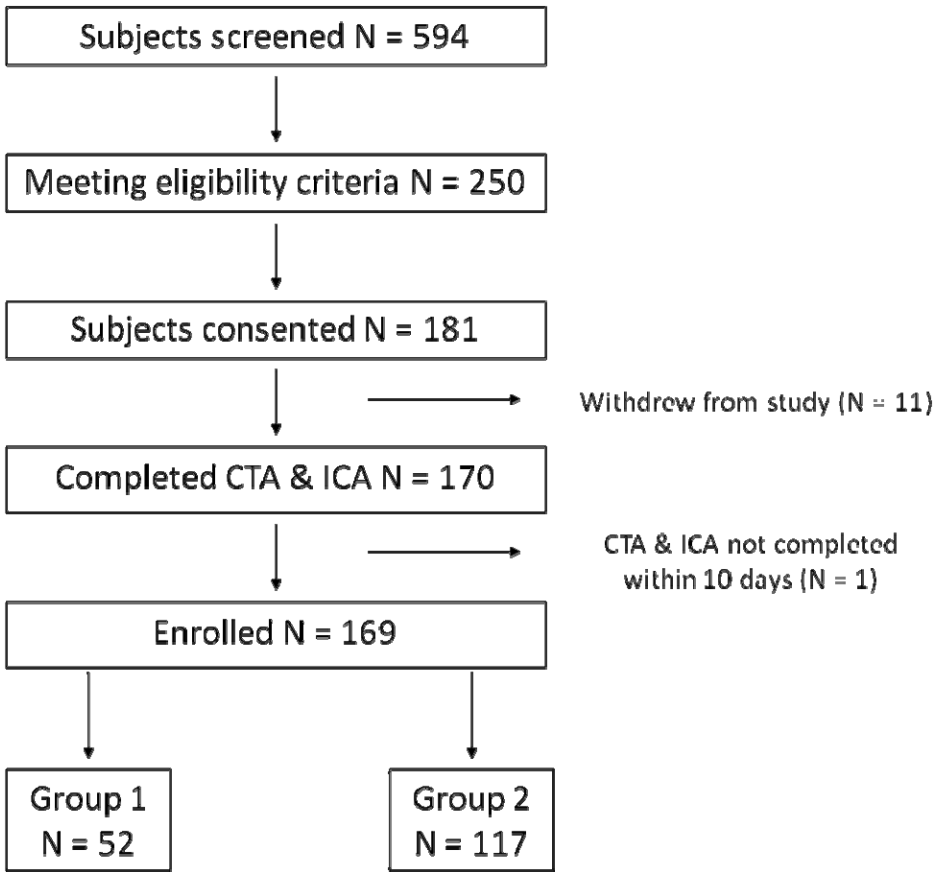
variables and Fisher's exact test was used for categorical variables. Diagnostic operating characteristics were presented as sensitivity, specificity, negative predictive value, positive predictive value, positive and negative likelihood rations as well as area under the receiver operating characteristic curves (ROC). Primary analysis was to examine the diagnostic accuracy at detecting ≥50% coronary artery stenosis for the overall study population and for each of the two groups evaluated in the study. Similarly a secondary analysis was completed for determining the diagnostic accuracy at detecting ≥70% coronary artery stenosis. Additionally, ROC were constructed for CTA to detect obstructive CAD. To examine the predictors of false CTA results, a post-hoc multiple logistic regression was conducted. The study was approved by each participating centres research ethics boards. The trial was registered through ClinicalTrials.gov, Identifier: NCT00371891.

Results

Study population

A total of 594 subjects were screened across the 4 participating centres. Of the 181 consenting subjects 11 individuals withdrew from the study prior to receiving the CTA. One subject's diagnostic results were not included in the analysis as greater than 10 days had lapsed between the two diagnostic tests. Following the above subject attrition, 169 subjects received both a CTA and ICA within 10 days, with 52 patients subjects recruited into Group 1 (presurgical evaluation) and 117 subjects (intermediate probability of CAD) in Group 2 (Figure 1).

Figure 1. Consort diagram for subject enrolment



The subjects enrolled in the study in both groups were primarily male (Group 1 = 75%; Group 2 = 59.8%), and with a mean overall age for both groups of 61.0 ± 10.4 years of age. The baseline characteristics of the subjects are presented in Table 1.

Table 1. Baseline subject characteristics

	Group 1 (N=52)	Group 2 (N=117)
Gender Male (N/%)	39 (75.0%)	70 (59.8%)
Mean age in years (SD), (min, max)	63.6 (11.4) (37.5, 85.5)	59.9 (9.9) (38.2, 87.2)
Mean BMI (SD) (min, max)	27.9 (4.9) (18.7, 43.3)	28.6 (5.2) (14.8, 43.0)
Hypertension (N/%)	25 (48.1)	63 (54.8)
Hyperlipidemia (N/%)	28 (54.9)	80 (68.4)
Diabetes (N/%)	8 (15.4)	24 (20.5)
Type I	1 (0.02)	2 (0.02)
Type 2	7 (0.13)	21 (0.2)
Current Smoker (N/%)	10 (19.2)	22 (18.8)
Former Smoker (N/%)	23 (44.2)	47 (40.2)
Congestive Heart Failure (N/%)	5 (9.6)	3 (2.6)
Peripheral Vascular Disease (N/%)	6 (11.5)	6 (5.1)
Cerebrovascular Disease (N/%)	5 (9.6)	5 (4.3)

As the subjects that were enrolled in the study were from two different patient populations, the factors present and presence of chest pain symptoms differed between the groups. The reasons for referral for ICA are presented for each group in Table 2. Of the 52 subjects enrolled into Group 1, the majority were referred for ICA for presurgical evaluation related to valvular heart disease (N=46) where as in Group 2 (N=117) the patients were referred due to chest pain syndrome, dyspnea and/or other symptoms such as syncope (Table 2).

Table 2. Factors present and chest pain symptoms at time of referral for conventional invasive coronary angiogram

	Group 1 (N=52)		Group 2 (N=117)	
	N	%	N	%
Chest Pain Syndrome	3	5.8	102	87.2
Dyspnea	35	68.6	61	52.1
Other - Syncope	-	-	15	12.9
Cardiomyopathy	3	5.8	0	-
Valvular Heart Disease	46	92.3	0	-
Aortic	29	73.0	0	-
Mitral	11	22.9	0	-
Aortic and Mitral Valve Disease	2	4.2	0	-
Other	4	8.3	0	-
Aortic Disease	1	1.9	0	-
Congenital	2	3.8	0	-
Number of symptoms at time of referral				
No symptoms / asymptomatic	33	63.5	21	17.9
One symptom / non-anginal	7	13.5	24	20.5
Two symptoms / atypical angina	4	7.8	32	27.4
Three symptoms / typical angina	8	15.4	40	34.1
Pretest Probability of CAD	28.3 (31.0) (0,100)		51.2 (28.4) (1.0, 96.0)	

* some patients may have presented with multiple symptoms and indications for coronary angiography

Non invasive CAD diagnostic evaluation for the subjects completing the study consisted of exercise stress tests, stress echocardiography or myocardial perfusion imaging. These tests were ordered completed as clinical indicated prior to referral for coronary angiography. The cardiac diagnostic tests completed are outlined in Table 3. In Group 2, some subjects received two or more diagnostic tests prior to ICA referral (27 (23%)).

Table 3. Diagnostic cardiac evaluation completed in subjects prior to ICA referral.

	Group 1 (N=52)		Group 2 (N=117)	
	N	%	N	%
Treadmill Test	9	17.3	50	42.7
Myocardial Perfusion Imaging	5	9.6	57	48.7
Stress Echocardiogram	7	13.5	16	13.7
Diagnostic Test Frequency				
None	31	59.6	25	21.4
One	21	40.4	65	55.5
Two	0	-	23	19.7
All Three	0	-	4	3.4

The radiation exposure related to both of CTA and ICA was documented throughout the study in order to compare the relative radiation doses between to two diagnostic modalities. The mean radiation exposure for CTA and ICA are outlined in Table 3. The mean radiation exposure from CTA was 61% greater than with ICA which was statistically significantly different ($P<0.001$).

Table 4. Comparative radiation dose exposure for CTA and ICA

	Group 1 (N=52)	Group 2 (N=117)
	Mean (SD), (min, max)	Mean (SD), (min, max)
CTA *DLP: dose length product (mGy*cm)*	1325.2 ± 414.9	1315.2 ± 291.2
Non-contrast (mSv)	1.39 (1.02) (0, 5.04)	1.42 (0.77) (0, 3.12)
Timing bolus (mSv)	0.76 (0.38) (0.27, 1.97)	0.62 (0.30) (0.22, 1.40)
Cardiac (mSv)	16.71 (5.70) (2.03, 43.27[a])	16.63 (3.96) (1.61, 27.87)
Total (mSv)	18.83 (5.81) (3.85, 44.56)	18.41 (4.08) (3.42, 29.76)
ICA *DAP: Dose Area Product (mGy*cm^2)*	55296 ± 30657	44399 ± 28247
Total (mSv)*	12.72 (7.05) (1.04, 29.56)	10.98 (7.84) (0.10, 48.05[b])

a. 1 person scanned twice (erratic heart rate)
b. Two scans with extended times and radiation doses: 1) 17 minutes, DAP=280930, 2) 8 minutes, DAP=150060

* P < 0.001 CT radiation dose equivalent was 61% greater than ICA

Diagnostic accuracy of CTA

The diagnostic accuracy of CTA as compared to ICA was determined for all subjects enrolled in the study and each of the groups individually. The primary analysis was for subject-based diagnostic accuracy to detect 50% or greater diameter stenosis. The sensitivity for CTA compared to ICA was 81.3% (95%CI: 71.0%,89.1%) and a specificity of 93.3% (95%CI: 85.9%,97.5%). A summary of the overall diagnostic operating characteristics is outlined in Table 5.

Table 5. Subject-based overall diagnostic accuracy of CTA vs. ICA at greater than or equal to 50% stenosis

CTA	ICA		Total
	Disease +	Disease -	
Disease +	65	6	71
Disease -	15	83	98
Total	80 (47.3%)	89	169
		95% CI (Lower)	95 % CI (Upper)
Sensitivity	81.3 %	71.0	89.1
Specificity	93.3 %	85.9	97.5
PPV	91.6 %	82.5	96.8
NPV	84.7 %	76.0	91.2
Positive Likelihood Ratio (LR+)	12.052	1.483	97.963
Negative Likelihood Ratio (LR-)	0.201	0.0272	1.4880
ROC: Area Under Curve	0.873	.	.

Similarly, the overall diagnostic accuracy of CTA compared to ICA to detect 70% or greater diameter stenosis was determined. The sensitivity for CTA was lower at 75.7% (95% CI: 64.0%,85.2%) while the specificity was similar 93.9% (95% CI: 87.3%,97.7%) as with other diagnostic operating characteristics (Table 6).

Table 6. Subject-based overall diagnostic accuracy of CTA vs. ICA at greater than or equal to 70% stenosis

CTA	ICA		Total
	Disease +	Disease -	
Disease +	53	6	59
Disease -	17	93	110
Total	70 (41.4%)	99	169
Statistic		95% CI (Lower)	95 % CI (Upper)
Sensitivity	75.7	64.0	85.2
Specificity	93.9	87.3	97.7
PPV	89.8	79.2	96.2
NPV	84.6	76.4	90.7
Positive Likelihood Ratio (LR+)	12.49	1.54	101.49
Negative Likelihood Ratio (LR-)	0.259	0.035	1.898
ROC: Area Under Curve	0.848	.	.

Diagnostic accuracy for CTA compared to ICA in both Group 1 and Group 2 to detect greater than or equal to 50% diameter stenosis were similar between the two groups with a CTA sensitivity of 81.8% (95% CI: 48.2%,97.7%) and specificity of 90.2% (95% CI: 76.9%,97.3%) in Group 1 (Table 7) and 81.2% (95% CI: 71.9%,89.6%) and specificity of 95.8% (95% CI: 85.7%,99.5%) in Group 2 (Table 8).

Table 7. Subject-based diagnostic accuracy of CTA vs. ICA at greater than or equal to 50% stenosis (Group 1).

CTA	ICA		Total
	Disease +	Disease -	
Disease +	9	4	13
Disease -	2	37	39
Total	11 (21.1%)	41	52
		95% CI (Lower)	95 % CI (Upper)
Sensitivity	81.8	48.2	97.7
Specificity	90.2	76.9	97.3
PPV	69.2	38.6	90.9
NPV	94.9	82.7	99.4
Positive Likelihood Ratio (LR+)	8.386	1.034	67.654
Negative Likelihood Ratio (LR-)	0.201	0.020	2.020
ROC: Area Under Curve	0.860	.	.

Table 8. Subject-based diagnostic accuracy of CTA vs. ICA at greater than or equal to 50% stenosis (Group 2).

CTA	ICA		Total
	Disease +	Disease -	
Disease +	56	2	58
Disease -	13	46	59
Total	69 (59.0%)	48	117
		95% CI (Lower)	95 % CI (Upper)
Sensitivity	81.2	71.9	89.6
Specificity	95.8	85.7	99.5
PPV	96.6	88.1	99.6
NPV	78.0	65.3	87.7
Positive Likelihood Ratio (LR+)	19.48	18.17	20.88
Negative Likelihood Ratio (LR-)	0.197	0.027	1.453
ROC: Area Under Curve	0.885	.	.

Examination of diagnostic operating characteristics across centres demonstrated differences in apparent diagnostic accuracy between the centres enrolling subjects in the study. The observed diagnostic accuracy of CTA compared to ICA in different centres provided different estimates of the sensitivity and specificity of the CTA. The sensitivity ranged from 93% (95%CI: 81%-99%) to 50% (16%-84%). There were also apparent differences in the baseline pre-test probability of CAD and overall prevalence of CAD between centres that enrolled subjects in the study (Table 9).

Table 9. Subject-based overall diagnostic accuracy of CTA vs. ICA at greater than or equal to 50% stenosis by enrolling centre.

	N	TP	FN	TN	FP	Sensitivity % (95% CI)	Specificity % (95% CI)	Pre-test Probability of CAD*	Prevalence CAD %
Overall	169	65	15	83	6	81 (71, 89)	93 (86, 98)	44.6%	47.3%
Centre 1	102	41	3	54	4	93 (81, 99)	93 (83, 98)	39.2%	43.1%
Centre 2	40	11	4	23	2	73 (45, 92)	92 (74, 99)	43.8%	37.5%
Centre 3	11	4	4	3	0	50 (16, 84)	100 (29, 100)	58.9%	72.7%
Centre 4	16	9	4	3	0	69 (38, 91)	100 (29, 100)	73.6%	81.2%

TP=true positive; FN= false negative; TN=true negative; FP=false positive

In a post-hoc regression analysis using both univariate and multivariate regressions, factors predicting a false CTA result (false positive or false negative) included enrolling centre 1 versus other centres (OR: 0.313, P=0.033), the pre-test likelihood of CAD (OR 1.019 P=0.005) and the presence of calcium on CTA (OR: 1.092, P=0.033). When considering the multivariate analysis only the centre effect remained as a predictor of false CTA results (OR: 0.283 P=0.005). The elimination of the centre effect from the multivariate regression model identified only one factor, (i.e.pre-test probability of CAD) as a significant predictor of false CTA reads (OR: 1.017, P=0.016).

Discussion

The diagnostic operating characteristics of CTA observed in the OMCAS study resulted in a lower sensitivity than was initially reported in published studies at the time of the study request by OHTAC. In a study by Raff *et al.,* patients scheduled to have elective invasive coronary angiography for suspected coronary artery disease, 64-slice CTA was found to be accurate in assessing CAD when compared to ICA as outlined in table 10.[19] This study however also identified a reduced accuracy of CTA in patients with extensive coronary calcification, higher heart rates and obesity.[19] Other evaluations have also been conducted using CTA and as with Raff *et al*. these studies are primarily in patients with suspected CAD.[20-23] Many of the initial studies examining the clinical efficacy of CTA in comparison to CCA often involve patients that were high risk and already scheduled for a CCA[5]. This poses itself as an issue in the real world since the primary use of this test occurs in low to intermediate prior probability of CAD risk.[24]

Several studies have been published since 2006, when the initial OHTAC review and OMCAS clinical protocol were completed, that have examined the diagnostic accuracy of CTA in patients with comparable subject characteristics (low-intermediate probability of CAD) to those found in this study. Many of these evaluations have been conducted in a single centre with a few multicentre studies similar to OMCAS (Table 10).

Table 10. Comparison OMCAS with results with published studies

	N	TP	FN	TN	FP	Sensitivity % (95% CI)	Specificity % (95% CI)	Prevalence CAD %	Sites	Core Lab
Low to intermediate probability of CAD										
Raff (2005)[19]	70	38	2	27	3	95 (88, 98)	90 (80, 94)	57%	Single	No
Oncel (2007)[25]	80	62	0	18	0	100 (97, 100)	100 (90, 100)	78%	Single	No
Cademartiri (2007)[26]	72	20	0	51	1	100 (83, 100)	98 (89, 99)	28%	Single	No
Meijboom (2007)[27]	149	44	0	93	12	100 (93, 100)	89 (86, 89)	30%	Single	No
Herzog (2007)[28]*	55	19	0	30	6	100 (85, 100)	83 (67, 94)	35%	Single	No
Ropers (2007)[29]	97	39	1	47	10	98 (87, 100)	82 (71, 90)	41%	Single	No
Budoff (2008)[30]*	227	52	3	142	30	95 (86, 98)	83 (80, 84)	24%	16 US sites	Yes
Husmann (2008)[31]	63	23	3	31	6	89 (76, 96)	84 (75, 89)	41%	Single	No
Piers (2008)[32]	60	38	0	10	12	100 (94, 100)	55 (43, 55)	63%	Single	No
Miller (2008)[33]*	291	139	24	115	13	85 (79, 90)	90 (83, 94)	56%	9 Int'l sites	Yes
OMCAS	169	65	15	83	6	81 (71, 89)	93 (86, 98)	47%	4 Ont. sites	No
Intermediate to high Probability of CAD										
Shabestari (2007)[34]*	138	104	4	20	10	96 (91,99)	67 (47,83)	78%	Single	No
Shapiro (2007)[35]*	37	28	1	5	3	97 (82, 100)	63 (24, 91)	78%	Single	No
Meijboom (2008)[36]*	360	244	2	73	41	99 (98, 100)	64 (55,73)	68%	3 Sites	No

* studies included in Medical Advisory Secretariat analysis

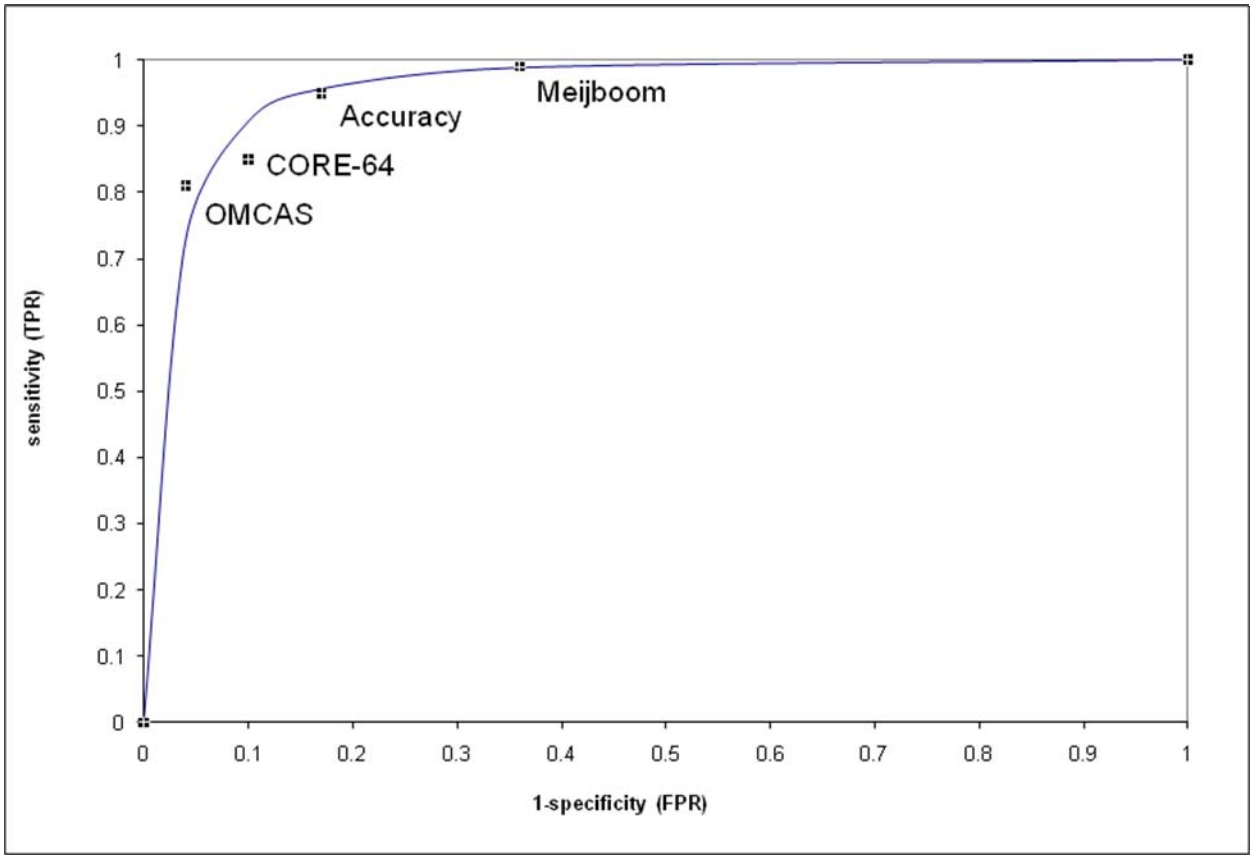
Multicentre studies measuring the diagnostic accuracy of CTA compared to ICA have demonstrated a high sensitivity for the test ranging from 85.5-99.0%. However, in regards to specificity, the results range from 64.0% – 90.0% (Table 10 and 11).[30,33,36]

Table 11. Methodological characteristics of other multicentre studies comparing CTA to ICA

Study Characteristic	OMCAS (2010) (N=169)	Miller (2008) (CORE 64) (N=291)	Budoff (2008) (ACCURACY) (N=230)	Meijboom (2008) (Netherlands) (N=360)
Number of centres	4	9	16	3
Multiple vendors	Yes	No	No	Yes
Within centre reading	Yes	No	No	No (switched)
Number of CTA readers	9	2	3	6
Number of ICA readers	12	n.r.	1	3

The OMCAS differed in its methodology from the other multicentre trials in that it was designed to mimic as close as possible daily clinical diagnostic activities without the use of a core lab (i.e within centre reading of images) and including multiple CTA vendors and multiple readers of CTA and ICA. In addition the evaluation of both CTA and ICA were completed by the clinicians participating in the study as per usual care. The one exception is that duplicate reads were completed for each test and where disagreement occurred a third read was conducted. The receiver operating curve incorporating the study results from each of the multicentre studies compares the diagnostic operating characteristics from OMCAS in context to the other studies (Figure 2). The results from this study are aligned with the other multicentre studies, however, demonstrates a lower sensitivity and higher specificity relative to the other trials.

Figure 2. Receiver operating curve (ROC) for multicentre studies comparing CTA to ICA



The lower overall sensitivity found in this study may be related to several factors including centre differences in patient related parameters and by centre specific factors. The differences in patient baseline pre-test probability of CAD accompanied by differences in reading styles and visual thresholds for abnormal studies may have resulted in some of the centre variation found in the study. In addition, CTA procedure differences such as final contrast infusion rates (although specified in the protocol), image acquisition protocols and the availability of dedicated personnel to perform CTA may have contributed to the lower sensitivity found in this study as compared to other multicentre trials.

From a patient safety perspective the radiation exposure found in this study for both CTA and ICA were higher that generally reported in other studies. These higher values

may reflect “real-world” practice patterns. It should be noted that since the enrolment of the subjects in this trial newer algorithms for CTA acquisition have been developed that can significantly reduce radiation exposure while maintaining image quality.

When examining the diagnostic operating characteristics of CTA it is therefore important to recognize that the results of a single centre may not necessarily be generalizable to all centres. Differences in local practice and protocols as well as experience and training associated with CTA need to be considered. This study was conducted in 4 academic teaching hospitals in Ontario with established CTA programs and protocols. The utilization of CTA should be accompanied by the establishment of acquisition protocols, patient criteria for which the diagnostic test is most suited and the understanding of downstream resource utilization and implications related to the use of other diagnostic modalities used for CAD.

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