Diagnostic accuracy of second-generation dual-source computed tomography coronary angiography with iterative reconstructions: a real-world experience

Accuratezza diagnostica dell’angiografia coronarica con tomografia computerizzata a doppia sorgente di seconda generazione con ricostruzioni iterative: valutazione nel mondo reale

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Abstract

Purpose. The authors evaluated the diagnostic accuracy of second-generation dual-source (DSCT) computed tomography coronary angiography (CTCA) with iterative reconstructions for detecting obstructive coronary artery disease (CAD).

Materials and methods. Between June 2010 and February 2011, we enrolled 160 patients (85 men; mean age 61.2±11.6 years) with suspected CAD. All patients underwent CTCA and conventional coronary angiography (CCA). For the CTCA scan (Definition Flash, Siemens), we used prospective tube current modulation and 70–100 ml of iodinated contrast material (Iomeprol 400 mgI/ml, Bracco). Data sets were reconstructed with iterative reconstruction algorithm (IRIS, Siemens). CTCA and CCA reports were used to evaluate accuracy using the threshold for significant stenosis at ≥50% and ≥70%, respectively.

Results. No patient was excluded from the analysis. Heart rate was 64.3±11.9 bpm and radiation dose was 7.2±2.1 mSv. Disease prevalence was 30% (48/160). Sensitivity, specificity and positive and negative predictive values
of CTCA in detecting significant stenosis were 90.1%, 93.3%, 53.2% and 99.1% (per segment), 97.5%, 91.2%, 61.4% and 99.6% (per vessel) and 100%, 83%, 71.6% and 100% (per patient), respectively. Positive and negative likelihood ratios at the per-patient level were 5.89 and 0.0, respectively.

**Conclusions.** CTCA with second-generation DSCT in the real clinical world shows a diagnostic performance comparable with previously reported validation studies. The excellent negative predictive value and likelihood ratio make CTCA a first-line noninvasive method for diagnosing obstructive CAD.

**Keywords** Computed tomography coronary angiography · Iterative reconstructions · Diagnostic accuracy · Dual-source computed tomography · Conventional coronary angiography · Coronary artery disease · Clinical value

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**Introduction**

Computed tomography coronary angiography (CTCA) has become a part of clinical practice for diagnosing obstructive coronary artery disease (CAD) [1–8]. Studies demonstrating the accuracy of 64-slice CTCA used, for the most part, validation methodologies [i.e. with conventional coronary angiography (CCA)] as a reference standard and in a high-risk population) [3–7, 9–18]. Few studies report its real efficacy in the clinical settings [19]. In those studies, diagnostic performance was lower than previously reported in the main studies of diagnostic accuracy [19]. Guidelines and international panels recommend using CTCA in patient populations at low to intermediate risk, where stress tests are inconclusive or cannot be performed [8, 20–22].

The introduction of new technologies with improved temporal, spatial and contrast resolution, such as the second-generation dual-source computed tomography (DSCT), offers the possibility of making the technique more reliable and robust. In addition, the introduction of iterative reconstruction algorithms provides improvement in image quality by significantly reducing image noise [19]. The aim of this study was to compare the diagnostic performance of CTCA using a second-generation DSCT system and iterative reconstructions with CCA in detecting obstructive CAD.

**Materials and methods**

**Study population**

From June 2010 to February 2011, 160 patients (85 men; 75 women) were prospectively enrolled in this study. The study population consisted of patients with chest pain suggestive of coronary artery disease, referred to our institution for diagnostic coronary angiography. Informed consent was obtained from all patients before enrollment in the study.

**Methods**

CTCA was performed using a second-generation DSCT system (Sensation 64, Siemens Healthcare, Forchheim, Germany) with a slice thickness of 0.625 mm. Reconstruction was performed with iterative algorithms to improve image quality. The CTCA was followed by CCA using conventional coronary angiography (CAG) as a reference standard.

**Results**

The diagnostic performance of CTCA was evaluated by comparing the results with CCA. The sensitivity, specificity, positive predictive value and negative predictive value of CTCA were 90.1%, 93.3%, 53.2% and 99.1% (per segment), 97.5%, 91.2%, 61.4% and 99.6% (per vessel) and 100%, 83%, 71.6% and 100% (per patient), respectively. Positive and negative likelihood ratios at the per-patient level were 5.89 and 0.0, respectively.

**Conclusions**

CTCA with second-generation DSCT in the real clinical world shows a diagnostic performance comparable with previously reported validation studies. The excellent negative predictive value and likelihood ratio make CTCA a first-line noninvasive method for diagnosing obstructive CAD.

**Keywords** Computed tomography coronary angiography · Iterative reconstructions · Diagnostic accuracy · Dual-source computed tomography · Conventional coronary angiography · Coronary artery disease · Clinical value
mean age, 61.2±11.6 years) with suspected CAD [chest pain and/or abnormal electrocardiogram (ECG) suggestive of myocardial ischaemia] and positive CCA were enrolled in the study. All patients underwent CTCA and CCA. Only patients with sinus rhythm who had never undergone percutaneous angioplasty or coronary artery bypass graft surgery and were able to maintain a breath-hold for at least 5 s were included. Patients with acute coronary syndrome, with absolute contraindications to intravenous administration of iodinated contrast material (e.g., known allergy, kidney failure or thyroid disorders) were excluded. The ethics committee approved the study, and all patients provided informed consent.

Patient preparation

Patients with a heart rate (HR) >60 bpm and without specific contraindications received a 5-mg intravenous dose of beta-blockers (atenolol, Tenormin, AstraZeneca). In the absence of contraindications, sublingual nitrate (dinitrate isosorbide, Carvasin 5 mg, Wyeth Lederle) was administered prior to the scan.

CTCA scan protocol and image reconstruction

The study was performed with a DSCT system with 128 (64×2×2) slices (Definition Flash, Siemens, Forchheim, Germany) [4, 5]. Two scans were performed in all patients: one to visualise coronary artery calcium (a) and one angiography scan (b). The following parameters were used for the scans [5, 19]:

a) Sequential scan protocol: Number of slices per rotation 62×2×2; gantry rotation time 280 ms; temporal resolution 75 ms; scan direction craniocaudal; reconstruction algorithm 180°; acquisition time window 70% of the RR interval; tube voltage 120 kV; tube current 150 mAs. Images were reconstructed with the following parameters: effective slice thickness 3 mm; reconstruction increment 1.5 mm; field of view (FOV) 150–160 mm; convolution kernel for calcium score (B35f).

b) Spiral scan protocol: Number of slices per rotation 62×2×2; slice thickness 0.6 mm; gantry rotation time 280 ms; temporal resolution 75 ms; scan direction craniocaudal; reconstruction algorithm 180°; patient table feed/pitch variable and adapted to HR (range 0.16–0.35); tube voltage 100–120 kV [according to patient body mass index (BMI)]; tube current 320–370 mAs (according to patient BMI); effective slice thickness 0.6–0.75 mm; reconstruction increment 0.4 mm; FOV 150–160 mm; convolution kernel medium smooth with first-generation iterative reconstruction (126–146f; IRIS, Siemens, Germany). This algorithm requires more time than conventional filtered back-projection reconstructions (three
images/second vs. 20 images/second). Prospective tube current modulation was used with a high-dose window from 65% to 80% of the RR interval and a MinDose protocol (Siemens, Germany) in the remaining phases of the cardiac cycle (i.e. 4% of maximum amperes; Fig. 1). Mean dose-length product was 517±153, which corresponds to an effective dose (conversion factor 0.014 mSv·mGy⁻¹·cm⁻¹ for the chest) of 7.2±2.1 mSv [7]. Between 70 ml and 100 ml of iodinated contrast material (Iomeprol, Iomeron 400, Bracco, Milan, Italy) was administered at an injection rate of 5–6 ml/s using an automatic injector (Stellant, MedRAD, Pittsburgh, PA, USA) attached to an 18- to 20-gauge needle cannula positioned in an antecubital vein [5].

Coronary artery enhancement was optimised by using the bolus-tracking technique (CARE bolus, Siemens, Forchheim, Germany) to synchronise contrast material arrival in coronary arteries with the beginning of the scan [5, 23]. Angiography scan data were obtained during a single breath-hold of 4–7 s (according to HR and adaptive pitch). Retrospective reconstructions based on the ECG signal were done on the angiography scans to obtain images free from motion artefacts in the maximum-dose time window (65–80% of the RR interval). The optimal diastolic phase was automatically obtained within this time window (Best-Phase, Siemens, Germany). Additional reconstructions in different reconstruction time windows of the cardiac cycle were analysed whenever this was considered necessary (e.g. in cases of persistent residual heart motion, which reduces the diagnostic quality of the images).

CTCA image evaluation

All CTCA images were evaluated in consensus by two readers with 10 and 5 years of experience, respectively, in the

b) protocollo di scansione spirale, numero di strati per ro-

tazione 62×2×2, spessore di strato 0,6 mm, tempo di ro-
tazione 280 ms, risoluzione temporale 75 ms, direzione
della scansione cranio-caudale, algoritmo di ricostru-
tione 180°, avanzamento per rotazione/pitch variabile
ed adattativo alla frequenza cardiaca (range 0,16–0,35),
voltaggio del tubo radiogeno 100–120 kV (a seconda
dell’indice di massa corporea [BMI] del paziente), po-
tenza del tubo radiogeno 320–370 mAs (a seconda del
BMI del paziente), spessore di strato effettivo ricostruito
0,6–0,75 mm, incremento di ricostruzione 0,4 mm, FOV
150–160 mm, filtro di convoluzione medium-smooth con
ricostruzione iterativa di prima generazione (I26f-I46f;
IRIS, Siemens, Germania). Tale algoritmo di ricostru-
tione richiede un tempo maggiore rispetto alla ricostru-
zioni convenzionali filtered back-projection (3 immagini/
secondo vs. 20 immagini/secondo). La modulazione pro-
spektiva dell’amperaggio del tubo è stata utilizzata con
una finestra di alta dose del 65% all’80% dell’intervallo
RR e protocollo MinDose (Siemens, Germania) nelle ri-
manenti fasi del ciclo cardiaco (ossia al 4% dell’ampe-
raggio massimale) (Fig. 1). Il dose length product (DLP)
medio delle scansioni è stato di 517±153 corrispon-
dente ad una dose efficace (fattore di conversione 0,014
mSv·mGy⁻¹·cm⁻¹ per il torace) di 7,2±2,1 mSv [7]. Sono
stati somministrati 70–100 ml di mezzo di contrasto io-
dato (Iomeprol, Iomeron 400, Bracco, Milano) alla velo-
cità di 5–6 ml/s mediante iniettore automatico (Stellant,
MedRAD, Pittsburgh, USA) collegato ad un’a Ago-cannula
da 18–20 gauge preventivamente posizionata in una vena
antecubitale [5].

Allo scopo di ottimizzare l’opacizzazione dei vasi arte-
riosi coronarici, è stata utilizzata la tecnica del bolus-tra-
cking (CARE bolus, Siemens, Forchheim, Germania) per
sincronizzare l’arrivo del mezzo di contrasto nelle arterie

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**Fig. 1** Scan protocol and dose modulation: The maximum dose is delivered from 65% to 80% of the RR interval. In the remaining phases, the tube current drops to 4% of the dose. Within this modulation phase, reconstruction window position can be chosen (width 75 ms). ECG, electrocardiogram.

**Fig. 1** Protocollo di scansione e modulazione della dose. La massima dose viene somministrata dal 65% all’80% dell’intervallo RR. Nelle rimanenti fasi il tubo passa al 4% della dose. All’interno di questa fase di modulazione è possibile scegliere la posizione della finestra di ricostruzione (ampiezza 75 ms). ECG, elettrocardiogramma.
Comparing reports archived in the hospital radiology information system for CTCA and CCA, respectively. Reports were drawn up immediately after the procedures. Mean reporting time was 10 min for CTCA and 8 min for CCA.

Lesions were considered significant if stenosis was ≥50% for CTCA and ≥70% for CCA. Accuracy was then calculated as sensitivity, specificity and positive and negative predictive values (PPV and NPV), with 95% confidence intervals (CI) calculated with binomial expansion. Disease prevalence and positive and negative likelihood ratios (LR+ and LR-, respectively) with 95% CI were also calculated. Comparison between CTCA and CCA was performed per segment, per vessel and per patient on the entire patient population. Statistical analysis was carried out with a dedicated software package (Statistical Package for the Social Sciences, version 11.5, SPSS Inc., Chicago, IL, USA).

Valutazione dell’immagine di CTCA

Tutte le scansioni CTCA sono state analizzate da due osservatori in consenso con 10 e 5 anni di esperienza nel settore, non a conoscenza dei risultati della CAG. Tutte le modalità convenzionali di visualizzazione sono state utilizzate dall’operatore (assiali, multiplanari, curve multiplanari [MIP], volume rendering [VR]) su una workstation dedicata con piattaforma software Cardiologica (SyngoVia, Siemens, Germania). L’operatore ha identificato i segmenti coronarici utilizzando una classificazione in 17 segmenti modificata da quella fornita dall’American Heart Association [24]. I segmenti sono stati classificati come senza stenosi significative (normali o con irregolarità della parete o con stenosi <50%) o con stenosi significativa (stenosi ≥50%), utilizzando le classificazioni comunemente applicate [3, 6, 7].

Coronarografia convenzionale (CAG)

La CAG è stata eseguita entro 2 settimane dalla CTCA con tecnica convenzionale. L’operatore era a conoscenza dei dati derivanti dal referto e dalle immagini relative alla CTCA. L’operatore ha identificato i segmenti coronarici utilizzando una classificazione in 17 segmenti modificata da quella fornita dall’American Heart Association [24]. Tutti i segmenti, senza limiti di diametro, sono stati inclusi per il confronto con la CTCA. I segmenti sono stati classificati come senza stenosi significative (normali o con irregolarità della parete o con stenosi critica <70%) o con stenosi significative (stenosi critica ≥70%; nel caso del tronco comune ≥50%), utilizzando le classificazioni convenzionali e linee guida. Le stenosi coronariche sono state valutate dall’operatore durante la seduta angiografica nella proiezione di massima stenosi mediante valutazione visiva. La dose efficace media per la CAG (solo procedure diagnostiche) è risultata 5,6±3,8 mSv.

Conventional coronary angiography

CCA was performed within 2 weeks of the CTCA examination using a conventional technique. The operator was aware of data from the CTCA report and images and identified coronary artery segments using the modified American Heart Association (AHA) 17-segment classification [24]. All segments regardless of diameter were included in the comparison with CTCA. Segments were classified as being without significant stenosis (normal or with wall irregularities or stenosis <50%) or with significant stenosis (stenosis ≥50%) using the commonly applied classifications [3, 6, 7].

Statistical analysis

The diagnostic performance of CTCA was evaluated by comparing reports archived in the hospital radiology information system for CTCA and CCA, respectively. Reports were drawn up immediately after the procedures. Mean reporting time was 10 min for CTCA and 8 min for CCA.

Lesions were considered significant if stenosis was ≥50% for CTCA and ≥70% for CCA. Accuracy was then calculated as sensitivity, specificity and positive and negative predictive values (PPV and NPV), with 95% confidence intervals (CI) calculated with binomial expansion. Disease prevalence and positive and negative likelihood ratios (LR+ and LR-, respectively) with 95% CI were also calculated. Comparison between CTCA and CCA was performed per segment, per vessel and per patient on the entire patient population. Statistical analysis was carried out with a dedicated software package (Statistical Package for the Social Sciences, version 11.5, SPSS Inc., Chicago, IL, USA).

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Analisi statistica

La performance diagnostica della CTCA è stata valutata confrontando i referti archivati nel sistema informatico dell’ospedale per la CTCA e per la CAG, rispettivamente. Detti referti sono stati stilati immediatamente dopo le procedure. Per la CTCA il tempo medio di refertazione è stato di 10 min mentre per la CAG è stato di 8 min.

Le lesioni sono state considerate significative se ≥50% per la CTCA e se ≥70% per la CAG. L’accuratezza diagnostica è stata quindi calcolata come sensibilità, specificità, valore predittivo positivo e negativo con intervalli di confidenza del 95% calcolati con espansione binomiale. Sono stati inoltre calcolati la prevalenza di malattia, ed i likelihood ratio positivo e negativo (LR+ e LR-, rispettivamente) con intervalli di confidenza del 95%. Il confronto tra CTCA e CAG è stata eseguita per-segmento, per-vaso e per-paziente su tutta la popolazione. Le analisi statistiche sono state eseguite con un software dedicato (Statistical Package for the Social Sciences, versione 11.5, SPSS Inc., Chicago, Illinois).

Risultati

Nessun paziente o segmento è stato escluso dall’analisi. Il 95% dei pazienti (152/160) ha ricevuto il β-blockante aggiuntivo per via endovenosa. La frequenza cardiaca media ottenuta è risultata 64,3±11,9 bpm. Le caratteristiche dei pazienti sono mostrate nella Tabella 1. La prevalenza di malattia è risultata pari al 30%. In Tabella 2 sono riportate le prevalenze di malattia coronarica alla CAG. Il 70% (112/160) dei pazienti non aveva stenosi critiche dimostrabili alla CAG. Circa un decimo dei pazienti aveva malattia monovasale (9,4%; 15/160), e uno su venticinque aveva malattia trivasale (3,8%; 6/160). Il calcium score coronarico secondo Agatston è risultato intermedio con ampia variabilità (media±deviazione standard [DS]=178,6±346,1; media=17; range=0–2123), rispecchiando una popolazione eterogenea ed con prevalenza di malattia coronarica medio-bassa. L’accuratezza diagnostica della CTCA nell’individuazione delle lesioni significative con valutazione per-segmento, per-vaso e per-paziente è mostrata in Tabella 3 e nelle Figure 2–4. I valori di accuratezza diagnostica sono risultati paragonabili a quelli delle casistiche di validazione riportati nella letteratura[7, 14–16, 18, 25–27].

Valutazione per segmento

Sono stati inclusi per il confronto con la CAG 2471 segmenti. Di questi, 192 (7,8%) mostravano stenosi critiche alla CAG (Figg. 1 e 2). La CTCA ha generato 152 falsi positivi e 19 falsi negativi. Questo ha determinato dei valori di sensibilità del 90% e specificità del 93%.

Table 1 Description of the study population

<table>
<thead>
<tr>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Age (years; mean±SD)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
</tr>
<tr>
<td>Stable angina, n (%)</td>
</tr>
<tr>
<td>Atypical chest pain, n (%)</td>
</tr>
<tr>
<td>Silent ischaemia, n (%)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
</tr>
<tr>
<td>Hypercholesterolaemia, n (%)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
</tr>
<tr>
<td>Cigarette smoking, n (%)</td>
</tr>
<tr>
<td>Family history, n (%)</td>
</tr>
<tr>
<td>Obesity (BMI≥30 kg/m²; %)</td>
</tr>
<tr>
<td>Calcium score (Agatston; mean±SD)</td>
</tr>
<tr>
<td>Heart rate (bpm; mean±SD)</td>
</tr>
<tr>
<td>LVEF (%; mean±SD)</td>
</tr>
</tbody>
</table>

$SD$, standard deviation; $M/F$, males/females; $BMI$, body mass index; $bpm$, beats per minute; $LVEF$, left ventricle ejection fraction
a prevalence was 30% (Table 2). A total of 70% (112/160) of patients had no critical stenoses at CCA. Approximately one tenth of patients had single-vessel disease (9.4%, 15/160), and one in 25 had three-vessel disease (3.8%, 6/160). Agatston calcium score was intermediate, with ample variability (mean ± standard deviation [SD] 178.6 ± 346.1; median 17; range 0–2,123), thus revealing a heterogeneous population with a medium- to low prevalence of CAD. CTCA accuracy for identifying significant lesions with a per-segment, per-vessel and per-patient evaluation is reported in Table 3 and Figs. 2–4. Accuracy values are comparable with those of validation series reported in the literature [7, 14–16, 18, 25–27].

Per-segment evaluation

A total of 2,471 segments were included in the comparison with CCA. Of these, 192 (7.8%) showed critical stenosis (Figs. 1 and 2). There were 152 false positives and 19 false negatives at CTCA. This produced a sensitivity of 90% and specificity of 93%.

Per-vessel evaluation

A total of 637 coronary artery vessels were included in the evaluation. Of these, 80 (12.4%) showed critical stenosis at CCA. There were 49 false positive and two false negative results at CTCA. This produced a sensitivity of 98% and specificity of 91%. The best accuracy values were recorded in the left main coronary artery and the left anterior descending coronary artery (sensitivity 100%).

Per-patient evaluation

A total of 160 patients were included in the comparison with CCA. Of these, 48 (30.0%) showed at least one critical stenosis at CCA (Figs. 5 and 6). There were 19 false positive and 0 false negative results at CTCA. Accuracy values were excellent, with a sensitivity and NPV of 100%.

Discussion

Validation studies conducted to date focused on patient populations with a high pretest probability of CAD (range 50–90%) who were already candidates for CCA [3–7, 9–18]. Recommendations for the clinical use of CTCA suggest that it is appropriate to use the technique in cases in which the patient is at low to intermediate risk and stress tests are doubtful, inconclusive or cannot be performed [8, 20, 22]. Findings of our study show accuracy values in the

<table>
<thead>
<tr>
<th>Type of disease</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>No or non significant disease, n (%)</td>
<td>112 (70)</td>
</tr>
<tr>
<td>Single-vessel disease, n (%)</td>
<td>15 (9.4)</td>
</tr>
<tr>
<td>Two-vessel disease, n (%)</td>
<td>13 (8.1)</td>
</tr>
<tr>
<td>Three-vessel disease, n (%)</td>
<td>6 (3.8)</td>
</tr>
<tr>
<td>Total, n</td>
<td>160</td>
</tr>
</tbody>
</table>
Table 3 Diagnostic accuracy. Criterion used to compare techniques: lumen reduction $\geq 50\%$ in CTCA and $\geq 70\%$ in conventional coronary angiography (CCA) (except for the left main coronary artery, for which the criterion was $\geq 50\%$) assessed with direct vision. Accuracy values are presented in percentages, with the 95% confidence intervals calculated with binomial expansion in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sens.</th>
<th>Spec.</th>
<th>PPV</th>
<th>NPV</th>
<th>Prev.</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Per segment</strong></td>
<td>2,471</td>
<td>173</td>
<td>2,127</td>
<td>152</td>
<td>19</td>
<td>90.1 (84–93)</td>
<td>93.3 (92–94)</td>
<td>53.2 (47–58)</td>
<td>99.1 (98–99)</td>
<td>7.8 (11.5–15.9)</td>
<td>13.5 (0.069–0.16)</td>
<td></td>
</tr>
<tr>
<td><strong>Per vessel</strong></td>
<td>637</td>
<td>78</td>
<td>508</td>
<td>49</td>
<td>2</td>
<td>97.5 (91–99)</td>
<td>91.2 (88–93)</td>
<td>61.4 (52–69)</td>
<td>99.6 (98–99)</td>
<td>12.6 (8.46–14.51)</td>
<td>11.1 (0.006–0.1)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>160</td>
<td>19</td>
<td>120</td>
<td>20</td>
<td>1</td>
<td>95 (75–99)</td>
<td>85.7 (78–91)</td>
<td>48.7 (32–65)</td>
<td>99.2 (95–99)</td>
<td>12.5 (4.37–10.1)</td>
<td>6.6 (0.008–0.39)</td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>160</td>
<td>0</td>
<td>159</td>
<td>1</td>
<td>0</td>
<td>NA (96–99)</td>
<td>NA</td>
<td>100 (97–100)</td>
<td>0 (2.51–3.13)</td>
<td>0.106 (0.000–0.01)</td>
<td></td>
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</tr>
<tr>
<td>LAD</td>
<td>160</td>
<td>39</td>
<td>106</td>
<td>15</td>
<td>0</td>
<td>100 (90–100)</td>
<td>87.6 (80–92)</td>
<td>72.2 (58–83)</td>
<td>100 (96–100)</td>
<td>24.3 (5.02–12.95)</td>
<td>8.1 (0–NA)</td>
<td></td>
</tr>
<tr>
<td>CX</td>
<td>157</td>
<td>20</td>
<td>123</td>
<td>13</td>
<td>1</td>
<td>95.2 (76–99)</td>
<td>90.4 (84–94)</td>
<td>60.6 (42–77)</td>
<td>99.2 (95–99)</td>
<td>13.4 (5.88–16.85)</td>
<td>9.96 (0.007–0.35)</td>
<td></td>
</tr>
<tr>
<td><strong>Per patient</strong></td>
<td>160</td>
<td>48</td>
<td>93</td>
<td>19</td>
<td>0</td>
<td>100 (92–100)</td>
<td>83.0 (74–89)</td>
<td>71.6 (59–81)</td>
<td>100 (96–100)</td>
<td>30.0 (3.91–8.88)</td>
<td>5.9 (0–NA)</td>
<td></td>
</tr>
</tbody>
</table>

No., number; TP, true positive; TN, true negative; FP, false positive; FN, false negative; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio; RCA, right coronary artery; LM, left main coronary artery; LAD, left anterior descending artery; CX, circumflex coronary artery; HR, heart rate; NA, nonassessable.
In our study, fluctuations in accuracy values can be seen, with a high NPV (>99% in all cases), in the three levels of analysis, along with a progressive increase, from per-segment to per-vessel and per-patient analyses, in sensitivity (90%, 98%, 100%, respectively) and PPV (53%, 61%, 71%, respectively). The explanation for this fluctuation can be found in the clustering of obstructive coronary artery lesions. In some patients with obstructive disease, there may be more than one lesion, and it is more likely that at least one of the lesions is correctly interpreted if they are multiple in the individual patient.

The LR+ describes the extent to which the likelihood of disease increases when the test is positive, whereas the LR- describes the extent to which the likelihood of disease decreases when the test is negative. An excellent test of inclusion (sensitivity) should provide LR+ values > 10, while an excellent test of exclusion should provide LR- values > 10.
decreases when the test is negative. An optimal inclusion test (i.e. sensitivity) should provide LR+ values >10, whereas an optimal exclusion test (i.e., negative predictive value) should provide LR- values <0.10. In our case, the test is good for inclusion and excellent for exclusion. It should be noted that the use of CTCA as a first-line technique (i.e. before stress testing) does not rule out the use of stress tests but, rather, keeps them for cases in which CAD is subcritical/critical.

In our study, we used different thresholds for the level of stenosis significance in CTCA and CCA. This reflects the two modalities in daily practice. The result is nonetheless well known, being a reduction in specificity that depends in part on the modality and probably in part on the use of different thresholds. In addition to this is the fact that the absolute severity of stenosis is not strictly correlated with inducible ischaemia. This, in fact, depends on multiple factors that morphological evaluation alone of coronary arteries is unable to resolve. For this and clinical reasons, the patient with stenosis >50%, both in CTCA and CCA, should undergo stress imaging to precisely define the presence (valore predittivo negativo) dovrebbe fornire valori di LR-<0.10. Nel nostro caso il test risulta buono per inclusione ed ottimo per esclusione. Deve essere specificato che l’utilizzo della CTCA come metodica di prima istanza (prima dei test provocativi) non esclude l’effettuazione dei test di inducibilità ma la riserva ai casi in cui la malattia coronarica sia sub-critica/critica.

Nel nostro studio abbiamo utilizzato soglie diverse per la significatività delle stenosi in CTCA ed in CAG. Questo riflette la pratica quotidiana delle due rispettive metodiche. Il risultato rimane comunque quello conosciuto della riduzione della specificità che dipende in parte dalla metodica ed in parte, probabilmente, dall’utilizzo di soglie differenti. A questo va aggiunto che la severità assoluta della stenosi di per sé non identifica necessariamente la presenza di ischemia inducibile. Quest’ultima, infatti, dipende da fattori molteplici che la sola valutazione morfologica coronarica non è in grado di risolvere. Per questo motivo e per motivi clinici il paziente con stenosi >50%, sia in CTCA che in CAG, dovrebbe effettuare uno stress imaging per definire presenza, sede ed entità dell’ischemia inducibile.

Nel nostro studio un valore aggiuntivo hanno avuto le
In our study, an additional advantage was provided by using first-generation iterative reconstructions (IRIS, Siemens, Germany) that enable image noise to be significantly reduced without adjusting any other variables. Iterative reconstructions consist of a different and/or additional reconstruction technique to conventional reconstructions with filtered back-projection. The reconstructions require greater computing power and make it possible to obtain improved sampling of attenuation values of pixels/voxels in the image. The image matrix (i.e. 512×512) remains unchanged whereas an evident reduction in image noise is obtained, which increases the signal-to-noise ratio. Lastly, the radiation dose

**Fig. 5a-h** Negative CTCA. This 56-year-old, hypertense and dyslipidaemic man (body mass index 28) presented with atypical chest pain and abnormal electrocardiogram suggestive of ischaemia. CTCA (a-e) shows coronary arteries with no significant stenoses both in the volume-rendered images (a,b) and the curved multiplanar images (c: right coronary artery; d: left anterior descending coronary artery; e: circumflex coronary artery). CCA (f-h) confirms the absence of significant stenoses. The examination was performed with a heart rate of 58 bpm and a radiation dose of 8.9 mSv.

**Esempio di paziente con CTCA negativa.** Il paziente maschio iperteso e dislipidemico, di 56 anni (BMI=28), si presenta con dolore atipico e alterazioni elettrocardiografiche suggestive per ischemia. La CTCA (a-e) mostra coronarie esenti da stenosi significative sia nelle immagini con volume rendering (a,b) sia nelle immagini multiplano curvate (c coronaria destra; d coronaria discendente anteriore; e coronaria circonflessa). La coronarografia convenzionale (f-h) conferma l’assenza di stenosi significative. L’esame è stato condotto ad una frequenza cardiaca di 58 bpm con una dose di radiazioni di 8,9 mSv.

**Ricostruzioni iterative di prima generazione (IRIS, Siemens, Germania)** che consentono di ridurre significativamente il rumore dell’immagine a parità di altri parametri. Le ricostruzioni iterative consistono in una modalità differente e/o aggiuntiva di ricostruzione rispetto alla ricostruzioni convenzionali con retroproiezione filtrata. Tali ricostruzioni, richiedono una capacità di calcolo maggiore e consentono di ottenere un migliore campionamento del valore di attenuazione dei pixel/voxel all’interno dell’immagine. La matrice dell’immagine (512×512) non si modifica ma si ottiene una evidente riduzione del rumore dell’immagine che incrementa il rapporto segnale/rumore. Infine, la dose di radiazioni utilizzata nel presente studio è legata all’utilizzo di un protocollo con gating ECG retrospettivo e modulazio-
used in this study is based on a protocol with retrospective ECG gating and prospective dose modulation. This guarantees maximum performance of the CTCA technique. In addition, dose values of diagnostic CCA were similar to those of CTCA. There are now various dose-reduction techniques that have different configurations according to the protocol used. There are various protocols that enable a significant dose reduction by acquiring data in a single heart beat with a high-pitch prospective spiral acquisition. With this technique, the delivered dose is <1 mSv in optimal conditions, i.e. a regular heart rate <60 bpm in a patient with BMI<25 [25, 28]. Characteristics and conditions described pertain to a subgroup of the population that would normally undergo CTCA. However, dose reduction should be one of the fundamental aims in CTCA provided that it does not negatively impact the clinical performance of the diagnostic test.

**Fig. 6a-e** Positive CTCA. This 54-year-old, hypertense man (body mass index 26) with a family history of cardiovascular disease presented with atypical chest pain and abnormal electrocardiogram suggestive of ischaemia. CTCA (a-c) shows a left anterior descending coronary artery without significant stenosis (b) and a circumflex coronary artery with stenosis >50% in the context of a very irregular section of the wall (arrowhead, c). CCA (d,e) confirms stenosis of the circumflex artery (arrowhead, e). The examination was performed with a heart rate of 55 bpm and a radiation dose of 5.9 mSv.

**Fig. 6a-e** Esempio di paziente con CTCA positiva. Il paziente maschio iperteso con familiarità di 54 anni (BMI=26), si presenta con dolore tipico e alterazioni elettrocardiografiche suggestive per ischemia. La CTCA (a-c) mostra una coronaria discendente anteriore senza stenosi significative (b) ed una coronaria circonflessa con una stenosi >50% nel contesto di un tratto di parete molto irregolare (testa di freccia, c). La coronarografia convenzionale (d,e) conferma la stenosi della circonflessa (testa di freccia, e). L’esame è stato condotto ad una frequenza cardiaca di 55 bpm con una dose di radiazioni di 5.9 mSv.
affect the accuracy of the technique and, in particular, the NPV.

Limitations

CTCA and CCA reports can be interpreted as a limitation with respect to the more rigorous and semiquantitative/quantitative evaluations performed in validation studies. Nonetheless, this does provide a more realistic evaluation of the routine clinical impact of the technique. The fact that the CCA operator was aware of the CTCA findings is a limitation in terms of the validation. However, this algorithm is a reflection of clinical practice. Estimated radiation dose during CTCA (7.2±2.1 mSv) is comparable with that of diagnostic CCA in our series and others in the literature [29–34]. The heart rate of 64.3±11.9 bpm obtained in our population enabled a drastic dose reduction compared with previous technologies. A further reduction in mean and absolute HR could enable routine use of protocols with lower radiation doses without negatively affecting diagnostic performance. Indeed, using scan protocols with prospective ECG triggering could produce a further reduction in radiation dose. However, in the phases outside the maximum dose window (from 80% to 65% of the RR interval in our case), the dose is 4% with the protocol used (MinDose, Siemens, Germany), which enables evaluation of the ejection fraction and left ventricular wall motion (which otherwise cannot be performed).

Conclusions

The accuracy of CTCA with a second-generation DSCT system and using iterative reconstructions enables the technique to be used as a noninvasive anatomical reference test for the diagnosis and exclusion of obstructive CAD.

Conflict of interest None

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