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The role of detailed coronary atherosclerosis evaluation by CT in ischemic heart disease

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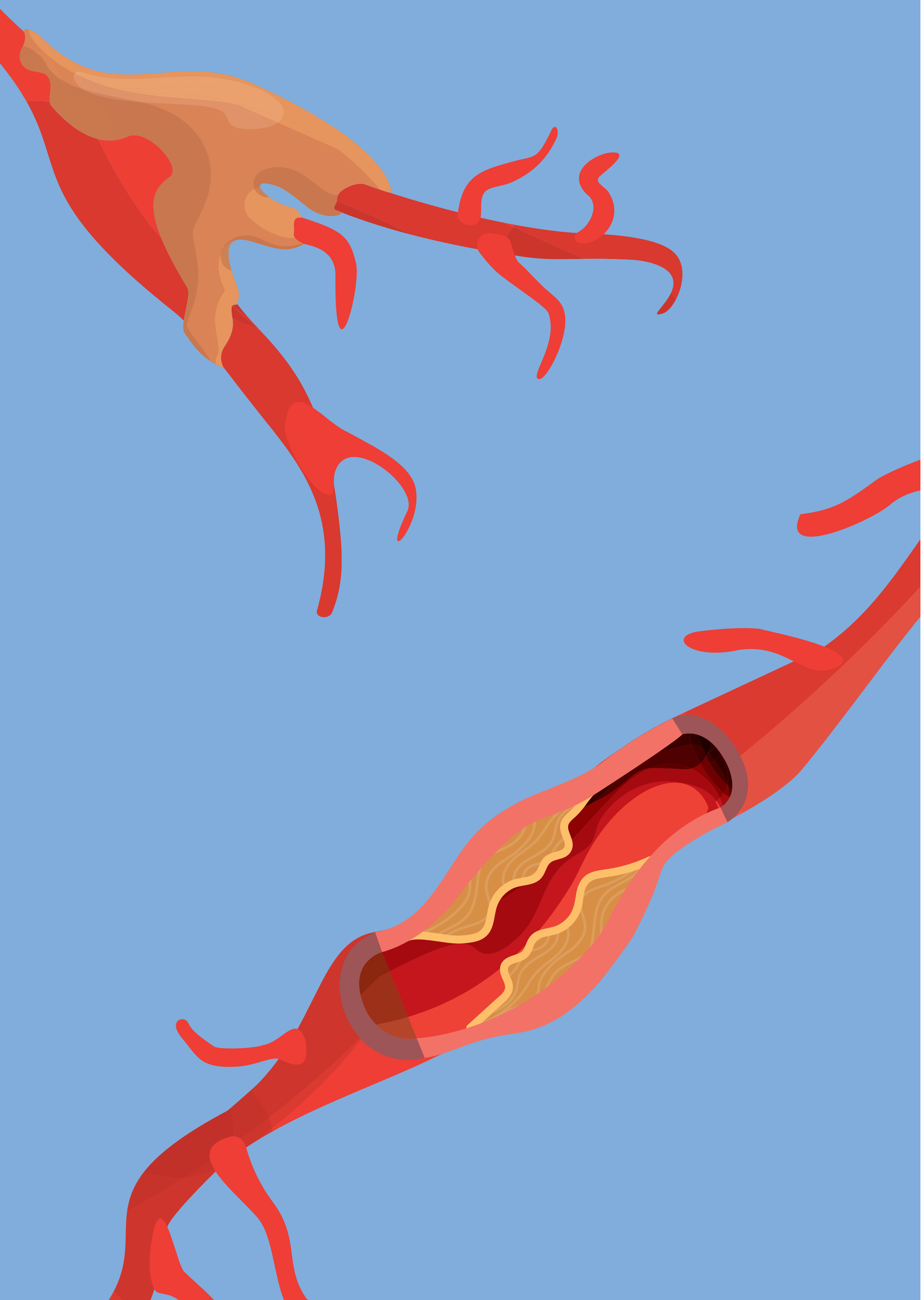

Chapter 10

Impact of computed tomography myocardial perfusion following computed tomography coronary angiography on downstream referral for invasive coronary angiography, revascularization and, outcome at 12 months

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Abstract

Aims

The aim of this study was to assess the impact of adding stress computed tomography (CT) myocardial perfusion (CTP) to coronary CT angiography (CTA) on downstream referral for invasive coronary angiography (ICA), revascularization, and outcome in patients presenting with new-onset chest pain.

Methods and results

Three hundred and eighty-four patients were referred for cardiac CT. Patients with lesions ≥50% stenosis underwent subsequently stress CTP. Perfusion scans were considered abnormal if a defect was observed in ≥ 1 segment. Downstream performance of ICA, revascularization, and the occurrence of major cardiovascular events (death, non-fatal myocardial infarction, and unstable angina requiring urgent revascularization) were assessed within 12 months. In total, 119 patients showed ≥50% stenosis on coronary CTA; stress CTP was normal in 61 patients, abnormal in 38 patients and was not performed in 20 patients. After normal stress CTP, 19 (31%) patients underwent ICA and 9 (15%) underwent revascularization. After abnormal stress CTP, 36 (95%) patients underwent ICA and 29 (76%) revascularizations were performed. Multivariable analyses showed a five-fold reduction in likelihood of proceeding to ICA when a normal stress CTP was added to a coronary CTA showing obstructive CAD. Major cardiovascular event rates at 12 months for patients with obstructive CAD and normal stress CTP ($N = 61$) were low: 1 myocardial infarction, 1 urgent revascularization, and 1 non-cardiac death.

Conclusion

The performance of stress CTP in patients with obstructive CAD at coronary CTA in the same setting is feasible and reduces the referral rate for ICA and revascularization. Secondly, the occurrence of major cardiovascular events at 12 months follow-up in patients with normal stress CTP is low.

Introduction

New-onset, chest pain often requires non-invasive cardiovascular imaging to assess the presence and extent of coronary artery disease (CAD), and to direct subsequent treatment[1]. Coronary computed tomography angiography (CTA) can reliably exclude obstructive coronary artery stenoses, but also has a high sensitivity for the detection of significant CAD.[2–5] However, in the recent PROMISE trial, coronary CTA guided treatment led to more invasive coronary angiographies (ICAs) and revascularizations without improving prognosis in comparison with functional testing.[2] Since coronary CTA only provides anatomical information of a coronary artery lesion (stenosis severity) it may be preferred to integrate this with functional evaluation of the lesion (ischaemia).

Functional information can nowadays be derived by stress CT myocardial perfusion (CTP) which has a high-diagnostic accuracy for assessing haemodynamically significant stenoses, as compared to ICA integrated with fractional flow reserve (FFR).[6–9] The clinical utility of combined coronary CTA and stress CTP and its impact on downstream referral for ICA is unknown. The present study aimed to investigate the impact of coronary CTA followed by stress CTP, when obstructive CAD (≥50% stenosis) is detected, on the downstream referral for ICA and revascularization in patients presenting with new-onset chest pain. Secondly, the occurrence of major cardiovascular events (death, non-fatal myocardial infarction, and unstable angina requiring urgent revascularization) was assessed within 12 months.

Methods

Patients

This study included patients who were referred by their general practitioners to the outpatient clinic of the cardiology department for the evaluation of CAD because of chest pain. Patients were subsequently referred for cardiac CT in the period March 2014 till October 2015. No haemodynamically unstable patients or patients referred from the emergency room were included. Contraindications were impaired renal function (glomerular filtration rate <60 mL/min), pregnancy, severe asthma or obstructive pulmonary disease, advanced atrioventricular block, or the presence of atrial fibrillation. Patients with a documented history of CAD [previous myocardial infarction (MI), percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG)], anomalous coronary arteries (as this interfered with the conventional reasons to perform stress CTP or ICA), uninterpretable coronary CTA or stress CTP were excluded.

Cardiac CT imaging protocol design

First, a routine coronary artery calcium (CAC) scan was performed in the majority of patients followed by coronary CTA in all patients. Directly after the acquisition of coronary CTA, the presence of obstructive CAD (≥50% stenosis) was evaluated on-site by an experienced physician. Only when obstructive CAD was detected, additional adenosine stress CTP was performed. The design of our cardiac CT imaging protocol is depicted in Figure 1. The treatment strategy after the stress CTP was left to the discretion of the referring cardiologist and hence, referrals for ICA were clinically indicated. Data were prospectively entered into the departmental electronic information system (EPD-Vision©, Leiden University Medical Center, The Netherlands). The Leiden University Medical Center's Institutional Review Board approved this retrospective evaluation of clinically acquired data and waived the need for patient written informed consent.

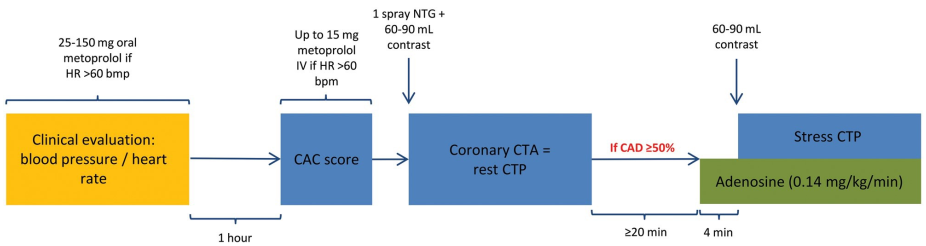


Figure 1. Cardiac CT imaging protocol. BPM, beats per minute; CAC, coronary artery calcium; CAD, coronary artery disease; CTA, computed tomography angiography; CTP, computed tomography perfusion; HR, heart rate; IV, intravenous; NTG, nitro-glycerine.

CT acquisition

A 320-row detector scanner (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan), with detector collimation of 320 × 0.5 mm, gantry rotation time of 350 ms, and temporal resolution of 175 ms was used. All patients were required to fast for 3 h and to abstain from caffeine 24 h prior to the CT acquisition in order to be able to proceed with the stress CTP, for which adenosine infusion is needed. If the heart rate was above 60 beats per minute (BPM), 25–150 mg oral metoprolol was administered 1 h prior to the CT acquisition and an additional intravenous dose (up to 15 mg) was given if the heart rate remained >60 bpm during the scout images, in absence of contraindications.

The data acquisition protocol consisted of the following: first, a non-contrast 120 kV scan was performed for calculation of the CAC score and to assess the needed coverage of the heart (120–160 mm) for the coronary CTA. Nitro-glycerine (0.4 mg) was sprayed sublingual prior to coronary CTA. Contrast agent (Iomeron 400, Bracco, Milan, Italy) was injected in a triphasic injection protocol: first, 50–90 mL (depending on patient weight) contrast agent (flow rate 5–6 mL/s), followed by 20 mL of a 1:1 mixture of contrast and saline and finally 25 mL of saline (flow rate 3 mL/s). Peak tube voltage was between 100 and 135 kV and tube current between 140 and 580 mA depending on body habitus. For coronary CTA, prospective ECG triggering was used to scan 70–80% of the R-R interval. In patients with a heart rate >65 bpm 30–80% of the R-R interval was scanned to allow for reconstructions of both the diastolic and systolic phases. Coronary CTA was acquired the next heart beat after the threshold of 300 Hounsfield units (HU) was reached in the descending aorta. Stress CTP was performed at least 20 min after finishing the coronary CTA to effectuate adequate myocardial contrast wash-out. The contrast bolus was infused after 4 min of continuous adenosine infusion (0.14 mg/kg/min) with electrocardiogram monitoring. Once the target threshold of 300 HU was reached in the descending aorta, stress CTP images were acquired the next one heart beat covering 80–99% of the R-R interval. Tube settings, injection protocol, scan range, and amount of contrast agent were similar for stress CTP and coronary CTA. The effective radiation dose was calculated by multiplying the dose-length product by 0.014 mSv/mGy/cm.[10]

Image reconstruction and analysis

All images were analysed with dedicated post-processing software (Vitrea FX 6.5; Vital Images, Minnetonka, Minnesota, USA) by two experienced physicians. All coronary arteries with a diameter ≥1.5 mm were analysed for obstructive CAD using a 17-segment model, as previously described.[11] For myocardial perfusion analysis, cardiac phases were reconstructed every 2% of the scanned interval from the rest data (same as coronary CTA) and stress data. The images were arranged in short axis, vertical long axis, and horizontal long axis with a slice thickness of 3 mm. All available phases were checked and the phase with the best quality was selected and interpreted for the presence of perfusion defects according to the 17-segment model.[12] A narrow window width and level (W300/L150) were used for the initial analysis and afterwards the observers could adjust the display settings. If a perfusion defect was observed, all other available phases were analysed to better differentiate between potential artefacts and true perfusion defects that indicate myocardial ischaemia or scar.[13] A CTP study was considered uninterpretable when artefacts hampered reliable assessment of myocardial enhancement throughout all phases. A stress CTP was considered normal if all myocardial segments showed normal myocardial enhancement and abnormal when a perfusion defect was observed in ≥1 segment. Perfusion defect severity was visually scored as follows: 1 = <30% transmurality, 2 = 30–50% transmurality, and 3 = >50% transmurality.[13] A summed stress/rest score was calculated by adding the defect severity scores of all myocardial segments.[14]

Invasive coronary angiography

ICA was performed according to standard protocols.[15] Each coronary segment was assessed for obstructive (≥50% stenosis) CAD by experienced interventional cardiologists. Cardiac CT results were available before the procedure. The performance of revascularization (PCI or CABG) among obstructive coronary lesions was based on the decision of the Heart Team.[16] FFR or intravascular ultrasound (IVUS) measurements were not systematically performed and therefore not used in the current analysis.

Follow-up

Downstream referral for ICA, the performance of coronary revascularization, the occurrence of death, myocardial infarction, and unstable angina requiring urgent revascularization were assessed within 3 and 12 months after the CT acquisition. Mortality data were gathered from the municipal civil registry and data regarding the other events were acquired by hospital files review and contacting patients. Non-fatal myocardial infarction and unstable angina were defined according to the standard definitions.[17,18]

Statistical analysis

Continuous variables were depicted as mean ± SD or median with 25–75% interquartile range (IQR), as appropriate. Normally distributed variables were compared with the independent samples t-test. Non-normally distributed variables were compared with the Mann–Whitney U test for two groups and with the Kruskal–Wallis test for multiple groups. Categorical variables were depicted as a number with percentage and compared with the chi-square test. Univariable and multivariable logistic regression analyses were performed to assess clinical and CT parameters that were most significantly related to obstructive CAD and downstream performance of ICA. Univariable associates with a P-value <0.05 were introduced in a multivariable analysis. Values were expressed as odds ratios (OR) with 95% confidence intervals (CIs). A P-value in a two-sided test <0.05 was considered statistically significant. All statistical analyses were performed with the use of IBM SPSS Statistics software (version 20, IBM Corp, Armonk, New York, USA).

Results

Patients

In total, 420 patients were referred for cardiac CT. For the present study, 36 patients were excluded because of: previous PCI, CABG, or MI (N = 16), anomalous coronary arteries (N = 8), uninterpretable coronary CTA (N = 7), and uninterpretable stress CTP (N = 5), as depicted in Figure 2. Hence, 384 patients (age 57.6 ± 11.4; 47% male) were included in the present study. Age (P < 0.001), diabetes mellitus (P < 0.001), hypertension (P < 0.001), hypercholesterolaemia (P < 0.001), and a family history of CAD (P = 0.029) were all significantly higher in patients who underwent coronary CTA and stress CTP (hence, having obstructive CAD) compared with only coronary CTA (Table 1). When entering these variables in a multivariable model, age: OR 1.05 (95% CI: 1.02–1.07, P < 0.001) per year, diabetes: OR 3.68 (95% CI: 1.90–7.12, P < 0.001) and hypertension: OR 1.76 (95% CI: 1.08–2.89) were independently associated with obstructive CAD.

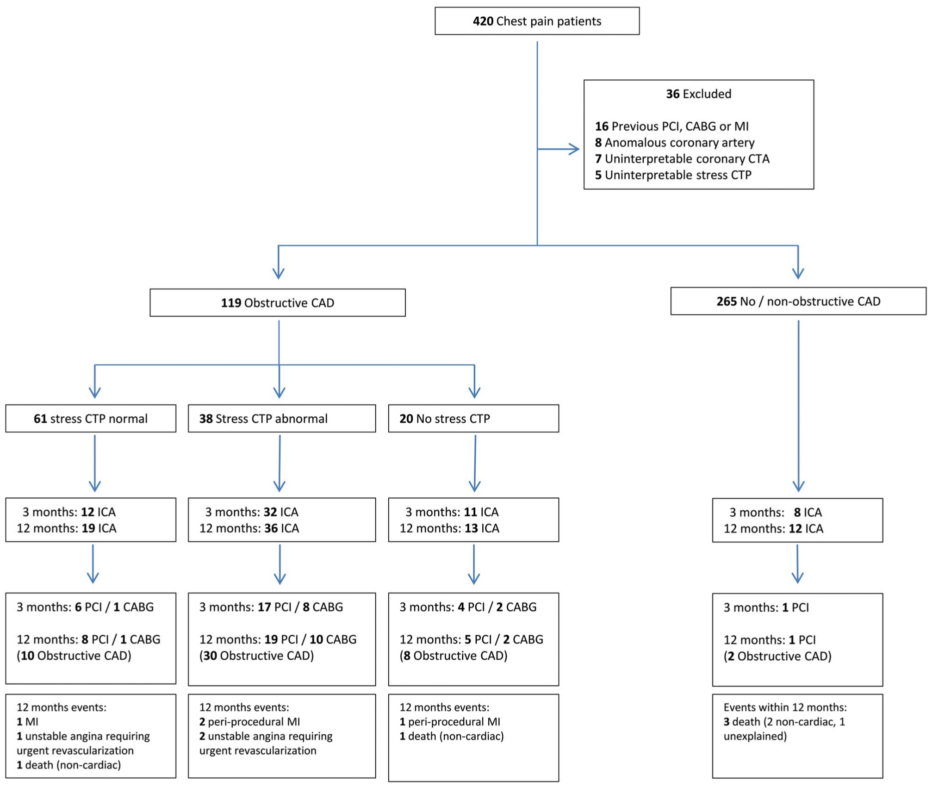


Figure 2. Flowchart. Flowchart demonstrating diagnostic testing and treatment strategies which the patients followed. CABG, coronary artery bypass graft; CAD, coronary artery disease; CTP, computed tomography perfusion; ICA, invasive coronary angiography; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 1. Patient characteristics

	Total (*N* = 384)	Only coronary CTA (*N* = 285)	Coronary CTA and stress CTP (*N* = 99)	*P*-value
Age (years)	57.6 ± 11.4	56.3 ± 11.6	61.3 ± 9.8	<0.001
BMI	27.0 ± 4.6	26.8 ± 4.8	27.5 ± 4.0	0.177
Male	179 (47)	126 (44)	53 (54)	0.109
CAC score[a]	15 (0–165)	1 (0–54)	232 (76–478)	<0.001
Cardiovascular risk factors				
Diabetes mellitus	54 (14)	24 (8)	30 (30)	<0.001
Hypertension[b]	172 (45)	111 (39)	61 (62)	<0.001
Hypercholesterolaemia[c]	107 (28)	61 (21)	46 (47)	<0.001
Family history of CAD[d]	169 (44)	116 (41)	53 (54)	0.029
Currently smoking	58 (15)	47 (17)	11 (11)	0.194
Medication				
Beta blocker	172 (45)	116 (41)	56 (57)	0.006
ACE-I/ARB	113 (29)	70 (25)	43 (43)	<0.001
Statin	124 (32)	74 (26)	50 (51)	<0.001
Diuretic	74 (19)	53 (19)	21 (21)	0.580
Calcium antagonist	46 (12)	31 (11)	15 (15)	0.264
Nitrate	26 (7)	18 (6)	8 (8)	0.547
Aspirin	85 (22)	54 (19)	31 (31)	0.011
Oral anticoagulant	29 (8)	16 (6)	13 (13)	0.015

Values are mean ± SD, median (IQR) or *n* (%).

ACE-I, angiotensin converting enzyme-inhibitor; ARB, angiotensin receptor blocker; BMI, Body Mass Index; CAC, coronary artery calcium; CAD, coronary artery disease; CTA, coronary computed tomography; CTP, computed tomography perfusion.

a Derived from respectively 363, 266, and 97 patients.

b Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or the use of antihypertensive medication.

c Defined as self-reported history of hypercholesterolaemia and/or therapeutic treatment with lipid lowering drugs.

d Presence of CAD in first degree family members at < 55 years in men and <65 years in women.

Cardiac CT imaging protocol findings

Ninety-nine patients underwent both coronary CTA and stress CTP and 285 patients underwent only coronary CTA. The median calcium score was 15 (IQR: 0–165), performed in 363 (95%) patients. Obstructive CAD was observed in 119 (31%) patients; 88 (73%) patients had 1-vessel disease, 17 (14%) 2-vessel disease, and 14 (12%) 3-vessel disease (Table 2). Of these patients with obstructive CAD, 20 patients did not undergo stress CTP because of: hypotension (N = 8), irregular heart rate (N = 5), adenosine induced advanced atrioventricular bock (N = 3), or logistic reasons (N = 4) (Figure 2). Of the remaining 99 patients, 61 (62%) stress CTP scans were normal and 38 (38%) were abnormal. Of the 38 abnormal stress CTP studies, the median summed stress score was 4 (IQR: 3–6) and the number of myocardial segments with hypoperfusion was 3 (IQR: 2–4). Of those 38 patients, 2 patients had a fixed defect (median summed rest score: 3) and 2 patients had a fixed defect and ischaemia (median summed difference score: 11). Three examples of patients with obstructive CAD and a perfusion defect on stress CTP are shown in Figure 3.

Mean heart rate during coronary CTA was 57.4 ± 10.9 bpm and 69.2 ± 14.6 bpm during stress CTP (Table 3). Two hundred twenty-one (58%) patients received an additional oral dose of beta blocker (mean 81 ± 33 mg) 1 h prior to the coronary CTA. Radiation exposure was 2.2 (1.5–3.4) mSv for coronary CTA, 3.1 (2.3–4.4) mSv for stress CTP. The dose for patients who underwent CAC scoring, coronary CTA, and stress CTP was 7.5 (5.6–9.8) mSv.

Table 2. Cardiac CT imaging protocol findings

	Total (*N* = 384)	Normal stress CTP (*N* = 61)	Abnormal stress CTP (*N* = 38)	No stress CTP (*N* = 285)	*P*-value
CAC score	15 (0–165)	156 (33–361)	430 (140–738)	1 (0–54)	<0.001
Coronary CTA					
No/non-obstructive CAD	265 (69)			265 (93)	
1 vessel ≥50% stenosis	88 (23)	51 (83)	25 (66)	12 (4)	<0.001
2 vessels ≥50% stenosis	17 (5)	6 (10)	6 (16)	5 (2)	<0.001
3 vessels ≥50% stenosis	14 (4)	4 (7)	7 (18)	3 (1)	<0.001

Values are median (IQR) or *n* (%).
CT, computed tomography; CTA, computed tomography angiography; CTP, computed tomography perfusion; IQR, interquartile range; CAC, coronary artery calcium.

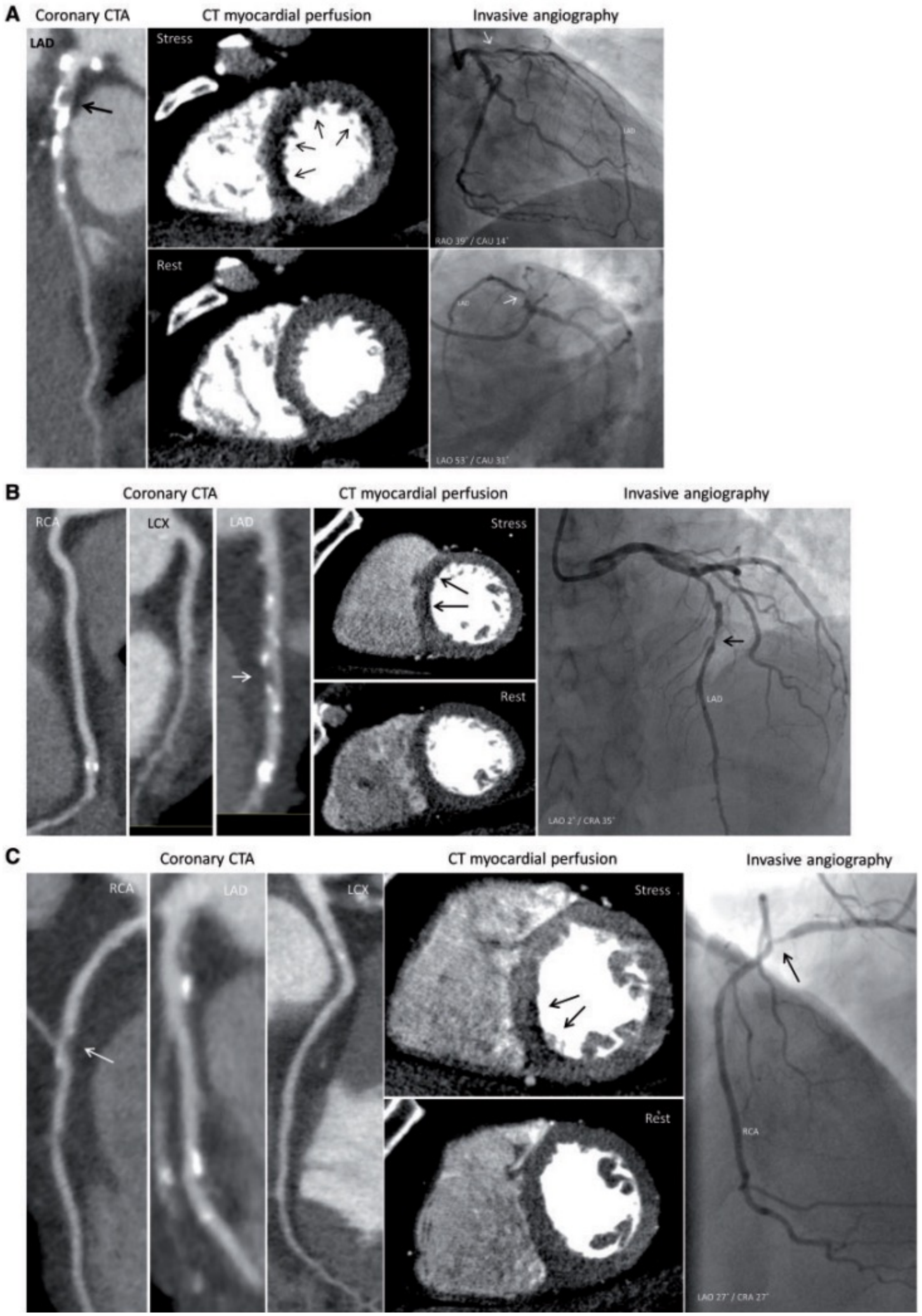
Table 3. CT acquisition parameters

	Coronary CTA (*N* = 384)	Stress CTP (*N* = 99)
Heart rate during acquisition, bpm	57.4 ± 10.9	69.2 ± 14.6
Administration of additional oral beta blocker prior to CT scan (%)	221 (58)	
Dosage of additional metoprolol, mg	81 ± 33	
Tube voltage, Kv	110 ± 12.7	
Tube current, mA	414 ± 112	
Contrast amount, mL	68 ± 11	69 ± 12
Radiation exposure, mSv (25–75% IQR)	2.2 (1.5–3.4)	3.1 (2.3–4.4)

CT, computed tomography; bpm, beats per minute; CTA, computed tomography angiography; CTP, computed tomography perfusion; IQR, interquartile range.

Invasive coronary angiography and revascularization

ICA was performed in 80 patients (21%) among whom 46 revascularizations (58%) were performed, consisting of PCI or CABG. The median time from CT acquisition to ICA was 1 month (IQR: 1–3 months). Figure 2 shows that the majority of ICA and revascularization procedures were performed within 3 months after the CT acquisition. Following coronary CTA without obstructive CAD (N = 265), 12 (5%) ICAs, and one PCI were performed at 12 months. The combination of extensive non-obstructive CAD and symptoms was the most important reason for ICA referral. Following obstructive CAD and normal stress CTP (N = 61), 19 (31%) patients underwent ICA among whom 9 (15%) revascularization procedures were performed (8 PCI; 1 CABG). The major reasons to proceed to ICA in these patients were persisting or worsening of symptoms. Revascularizations were performed based on: FFR <0.8 (n = 2), stenosis ≥ 70% (n = 4), or IVUS (N = 2; <4.0 mm2). Almost all, 36 (95%), patients with obstructive CAD and abnormal stress CTP (N = 38) underwent ICA of which 29 (76%) underwent revascularization (19 PCI; 10 CABG).



< Figure 3. Combined coronary CTA, CT myocardial perfusion, and invasive coronary angiography. **(A)** Coronary CTA demonstrates a severe lesion (>70%) in the proximal LAD (arrow). CT myocardial perfusion imaging shows extensive reversible ischaemia predominantly in the septal and anterior wall (arrows). ICA shows a severe lesion in the proximal LAD (arrow) which was stented. **(B)** Coronary CTA demonstrates non-obstructive CAD in the RCA and LCX and a moderate (50–70%) stenosis in the LAD (arrow). CT myocardial perfusion imaging shows ischaemia in the septal wall (arrows) and ICA confirmed the significant lesion in the mid-LAD (arrow) which was stented. (**C)** Coronary CTA shows a moderate (50–70%) stenosis in the mid-RCA (arrow) and non-obstructive CAD in the LAD and LCX. CT myocardial perfusion imaging shows ischaemia in the inferoseptal wall (arrow). ICA shows the significant stenosis in the RCA (arrow) which was stented. CTA, coronary computed tomography; CTP, computed tomography perfusion; ICA, invasive coronary angiography; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Multivariable analysis for invasive coronary angiography referral

Univariable associates that were significantly correlated with downstream performance of ICA were: age (OR: 1.04; 95% CI: 1.01–1.06; $P = 0.003$), diabetes mellitus (OR: 3.90; 95% CI: 1.21–7.17; $P < 0.001$), hypertension (OR: 3.30; 95% CI: 1.96–5.56; $P < 0.001$), hypercholesterolaemia (OR: 2.17; 95% CI: 1.30–3.64; $P = 0.003$), currently smoking (OR: 0.31; 95% CI: 0.12–0.81; $P = 0.017$), CAC score (OR: 1.70; 95% CI: 1.49–1.95; $P < 0.001$), and cardiac CT imaging protocol findings, as depicted in Table 4.

In multivariable analysis, only the cardiac CT imaging protocol findings and the calcium score remained significant determinants for ICA referral. An approximate five-fold reduction in likelihood of proceeding to ICA was observed when a normal stress CTP was added to obstructive CAD: obstructive CAD without stress CTP (OR: 18.67; 95% CI: 5.40–64.58; $P < 0.001$) vs. obstructive CAD + normal stress CTP (OR: 4.05; 95% CI: 1.57–10.45; $P = 0.004$). Furthermore, patients with obstructive CAD and abnormal stress CTP were likely to undergo subsequent ICA (OR: 227.21; 95% CI: 95.40.04–1289.34; $P < 0.001$).

Table 4. Patients characteristics and cardiac CT imaging protocol findings related to referral for ICA

	Univariable		Multivariable	
	Odds ratio (95% CI)	***P*-value**	**Odds ratio (95% CI)**	***P*-value**
Age	1.04 (1.01–1.06)	0.003	0.98 (0.94–0.98)	0.195
Male	1.45 (0.88–2.4)	0.144		
Cardiovascular risk factors				
Diabetes mellitus	3.90 (1.21–7.17)	<0.001	2.52 (0.96–6.64)	0.062
Hypertension	3.30 (1.96–5.56)	<0.001	1.76 (0.80–3.84)	0.160
Hypercholesterolaemia	2.17 (1.30–3.64)	0.003	0.52 (0.21–1.27)	0.148
Family history of CAD	1.34 (0.82–2.20)	0.244	1.37 (0.63–2.98)	0.434
Currently smoking	0.31 (0.12–0.81)	0.017	0.187 (0.04–0.886)	0.035
CT imaging protocol findings				
CAC score (Ln + 1)	1.70 (1.49–1.95)	<0.001	1.34 (1.10–1.62)	0.003
No/non-obstructive CAD	1 (–)		1 (–)	
Obstructive CAD without stress CTP	39.00 (13.16–115.55)	<0.001	18.67 (5.40–64.58)	<0.001
Obstructive CAD + normal stress CTP	9.50 (4.29–20.99)	<0.001	4.05 (1.57–10.45)	0.004
Obstructive CAD + abnormal stress CTP	378.00 (81.27–1758.18)	<0.001	227.21 (40.04–1289.34)	<0.001

Definitions as in Table 1. CT, computed tomography; CAC, coronary artery calcium; CAD, coronary artery disease; CTA, computed tomography angiography; CTP, computed tomography perfusion; CI, confidence interval.

Follow-up for cardiovascular events

During 1-year follow up, 3 events occurred in the obstructive CAD + normal stress CTP group (1 MI, 1 unstable angina requiring urgent PCI, 1 death (non-cardiac). Patients with obstructive CAD and abnormal stress CTP had 4 events: 2 peri-procedural MI during revascularization which was based on the CT results, 1 unstable angina while awaiting CABG, and 1 unstable angina requiring urgent PCI after the initial PCI which was based on the CT results. Patients with obstructive CAD without CTP had 1 death (non-cardiac) and 1 peri-procedural MI. Three patients with non-obstructive CAD experienced died (2 non-cardiac, 1 unexplained). Mortality information was complete for all patients. Follow-up information regarding MI and unstable angina requiring urgent revascularization were unavailable for 20 patients (5%): 3 patients with obstructive CAD + normal stress CTP (5%) and 17 patients with non-obstructive CAD (6%).

Discussion

The present study demonstrated the clinical feasibility of a cardiac CT imaging protocol consisting of a routine CAC score, coronary CTA, and adenosine myocardial stress CTP (in case of ≥50% stenosis), to guide downstream referral for ICA in patients presenting with new-onset chest pain. The gatekeeper function of a coronary CTA with no or non-obstructive CAD was reconfirmed; only 5% (12/265) of the patients were referred for ICA and one patient underwent revascularization. When obstructive CAD was observed, the addition of stress CTP could guide whether or not to refer a patient for ICA. After an abnormal stress CTP, 95% (36/38) of the patients was referred for ICA and after normal stress CTP 31% (19/61) underwent ICA. The revascularization rate within 12 months after abnormal stress CTP was high (76%, 29/38) and low after normal stress CTP: 15% (9/61). The occurrence of major adverse events was low after normal stress CTP (1 myocardial infarction, 1 urgent revascularization, and 1 non-cardiac death) indicating that it is safe to defer from ICA with regards to 12 months prognosis.

Integration of anatomical and functional non-invasive imaging

Non-invasive evaluation of patients presenting with stable chest pain can guide patient management in terms of discharge (in the absence of CAD), medical therapy or coronary revascularization. Coronary CTA is an excellent technique to exclude CAD, leading to increased clarification of the diagnosis of coronary heart disease compared with standard care, as shown in the SCOT-HEART trial.[3,19,20] Nevertheless, the presence of CAD on CTA does not provide information on the haemodynamic significance of these lesions (is there ischaemia or not?). Therefore, integration of anatomic imaging (coronary CTA) with functional imaging is needed to determine the optimal therapy (conservative, medical therapy or coronary revascularization). Indeed, results from the multi-centre PROMISE trial demonstrated that coronary CTA led to a substantial increase in ICAs (12.2% vs. 8.1%) and revascularizations (6.2% vs. 3.2%) compared with functional testing, without prognostic benefit.[2]

For this reason, use of integrated anatomic and functional imaging has gained popularity over the recent years, and significant experience has been obtained with hybrid imaging approaches that combine coronary CTA with myocardial perfusion imaging (MPI) using either single-photon emission computed tomography (SPECT) or positron emission tomography (PET).[21] These imaging modalities appeared highly accurate for detection of haemodynamically significant stenoses (as compared with ICA and FFR), and optimized referral for downstream invasive management in clinical practice.[22,23] Regarding hybrid imaging with coronary CTA and stress CTP, recent studies demonstrated good accuracy for detection significant CAD.[9,24–27]

Clinical experience with hybrid imaging techniques

Pazhenkottil et al.[22] performed coronary CTA and SPECT MPI in 318 patients for the evaluation of known or suspected CAD and assessed the rate of ICA and revascularization in the first 60 days after diagnostic testing. For patients with matched pathological findings (N = 51, having an obstructive stenosis on CTA with corresponding ischaemia on SPECT MPI), 61% (31/51) underwent ICA and 41% (21/51) underwent revascularization. For unmatched coronary CTA and SPECT MPI abnormalities, 20% (15/74) was referred for ICA and 11% (8/74) underwent revascularization. Similar results were shown by Fiechter et al.[28] who reported on 62 patients who underwent hybrid coronary CTA and cadmium-zinc-telluride imaging. All patients (n = 23) with matched pathological findings (obstructive stenosis on CTA with ischaemia on SPECT) underwent ICA with 91% (21/23) being revascularized. Moreover, 13% (5/39) of the patients with unmatched findings underwent ICA and 8% (3/39) was revascularized. Another study used hybrid 15O-water PET/CTA imaging in 375 patients.[29] Of patients with an obstructive stenosis and abnormal MPI, 88% (52/59) was referred for ICA and 58% (34/59) underwent revascularization. Patients with an obstructive stenosis on coronary CTA in combination with normal MPI were referred for ICA in 57% (31/54) and revascularization was performed in 15% (8/54).

In the current study, integrated anatomic and functional imaging was achieved by using CTA and stress CTP in a one-day protocol (one-stop shop). In 38 patients with matched pathological findings (obstructive stenosis on CTA and perfusion abnormalities on stress CTP) 95% (36/38) underwent ICA with 76% (29/38) being revascularized. Patients with obstructive stenosis on coronary CTA in combination with a normal stress CTP were referred for ICA in 31% (19/61) and revascularization was performed in 15% (9/61). Accordingly, the current findings with novel integrated coronary CTA/stress CTP confirm earlier results with SPECT/CTA or PET/CTA. Nevertheless, a substantial percentage of patients underwent PCI after a normal stress CTP in the current study. Of those 9 revascularizations only 2 were based on FFR (0.77 and 0.80) and the remaining on anatomical characteristics of the CAD (stenosis severity, plaque morphology). Hence, these lesions may have been functionally insignificant or, on the other hand, present myocardial ischaemia may not be detected with stress CTP.

FFRCT is another recently developed technique to derive functional information of coronary CTA detected lesions.[30] The recent multi-centre PLATFORM study assessed the impact of FFRCT on patient selection for ICA compared with standard care. It was demonstrated that the performance of FFRCT improved patient selection for ICA by showing high-revascularization rates per ICA compared with patients who directly underwent ICA (72%; 55/76 vs. 32%; 59/187).[31] However, the optimal functional imaging technique with CT (FFRCT or stress CTP) should be addressed in further studies with long term follow up.

Limitations

The single centre aspect of this study is a limitation. Although the absence of ischaemia on stress CTP convinced physicians to refrain from ICA in the majority of patients with obstructive CAD, it could be argued that these results demonstrate the adherence to stress CTP rather than the effectiveness of our cardiac CT imaging protocol. Nevertheless, few patients underwent ICA as yet after their treating physician initially refrained from ICA and events rates were low after normal stress CTP, indicating that ICA deferral is safe. In total, 17% of patients with obstructive CAD did not undergo stress CTP, which is a limitation. The use of beta blocker prior to stress testing is a debated topic as it may decrease the sensitivity to detect ischaemia.[32]

Conclusion

Stress CT myocardial perfusion impacts clinical decision making with regard to referral for ICA and revascularization. The occurrence of major cardiovascular events in patients with obstructive CAD and normal stress CT myocardial perfusion is low.

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