ORIGINAL ARTICLE

Current trends in patients with chronic total occlusions undergoing coronary CT angiography

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ABSTRACT

Objective Data describing the prevalence, characteristics and management of coronary chronic total occlusions (CTOs) in patients undergoing coronary CT angiography (CCTA) have not been reported. The purpose of this study was to determine the prevalence, characteristics and treatment strategies of CTO identified by CCTA.

Methods We identified 23 745 patients who underwent CCTA for suspected coronary artery disease (CAD) from the prospective international CCTA registry. Baseline clinical data were collected, and allocation to early coronary revascularisation performed within 90 days of CCTA was determined. Multivariable hierarchical mixed-effects logistic regression reporting OR with 95% CI was performed.

Results The prevalence of CTO was 1.4% (342/23 745) in all patients and 6.2% in patients with obstructive CAD (≥50% stenosis). The presence of CTO was independently associated with male sex (OR 3.12, 95% CI 2.39 to 4.08, p<0.001), smoking (OR 2.02, 95% CI 1.55 to 2.64, p<0.001), diabetes (OR 1.60, 95% CI 1.22 to 2.11, p=0.001), typical angina (OR 1.51, 95% CI 1.12 to 2.06, p=0.008), hypertension (OR 1.47, 95% CI 1.14 to 1.88, p=0.003), family history of CAD (OR 1.30, 95% CI 1.01 to 1.67, p=0.04) and age (OR 1.06, 95% CI 1.05 to 1.07, p<0.001). Most patients with CTO (61%) were treated medically, while 39% underwent coronary revascularisation. In patients with severe CAD (≥70% stenosis), CTO independently predicted revascularisation by coronary artery bypass grafting (OR 3.41, 95% CI 2.06 to 5.66, p<0.001), but not by percutaneous coronary intervention (p=0.83).

Conclusions CTOs are not uncommon in a contemporary CCTA population, and are associated with age, gender, angina status and CAD risk factors. Most individuals with CTO undergoing CCTA are managed medically with higher rates of surgical revascularisation in patients with versus without CTO.

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INTRODUCTION

Coronary CT angiography (CCTA) is a useful non-invasive tool that demonstrates high performance for diagnosis and prognosis of coronary artery disease (CAD).[1–3] Further, CCTA demonstrates precision for assessing the anatomical and morphological features of occluded coronary arteries, and has been successfully employed in the planning of chronic total occlusion (CTO) revascularisation.[4–6]

While the prevalence of CTO has been defined for individuals undergoing invasive coronary angiography,[7–10] data describing the prevalence and clinical characteristics of occluded coronary arteries among stable patients referred for non-invasive testing have not been reported to date. To this end, whether CTO influences the current management of CAD after non-invasive imaging remains unclear. The purpose of this investigation was to determine the prevalence of CTO in a consecutive multinational CCTA population and to provide detailed clinical and tomographic characteristics associated with CTO. The influence of CTO at the time of CCTA on treatment strategies was additionally examined.

METHODS

Study population

The CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry is an international multicentre observational registry collecting clinical, procedural and follow-up data of patients who underwent CCTA between 2005 and 2010 at 17 centres in 7 countries (USA, Canada, Germany, Switzerland, Italy, Austria and South Korea). A detailed description of the study design has been published elsewhere.[11] For the purpose of the present analysis, patients who underwent CCTA for suspected, but without prior known CAD, were included. The exclusion criterion of known CAD was defined as previous myocardial infarction and/or coronary revascularisation. Ethical approval was obtained from each of the study centres' institutional review board committees, and written informed consent was provided by the study participants.

The CONFIRM registry employs a standardised data collection method at all study sites to gather information regarding baseline cardiovascular risk factors, symptoms and medication before CCTA, as well as detailed angiographic results and clinical outcomes.[12] Pretest probability of CAD was defined using the Diamond–Forrester score,[13] and

symptom presentation was classified into the following categories: typical chest pain, atypical chest pain and non-cardiac pain.[14] Coronary artery calcium was quantified according to the method of Agatston. Details of this approach have been described elsewhere.[15]

Image acquisition and analysis

CCTA data acquisition was performed using at minimum a 64-slice CT scanner with the imaging protocol adhering to the Society of Cardiovascular Computed Tomography guidelines on appropriateness and performance of CCTA.[16] Dose-reduction strategies, including ECG-gated tube current modulation, reduced tube voltage and prospective axial triggering, were used whenever possible, with estimated radiation doses for CCTA ranging from 3 to 18 mSv.

Reconstructed data were evaluated in a uniform fashion across all study sites by level III-qualified readers using all necessary postprocessing techniques to determine the presence of CAD. Coronary segments were scored visually for the presence and composition of coronary plaque and degree of luminal stenosis with a 16-segment American Heart Association coronary artery model.[17] Plaque severity was graded on a per-segment, per-vessel and per-patient level. Plaque composition in each coronary segment was classified as non-calcified, partially calcified or calcified as defined elsewhere.[18] Coronary atherosclerotic lesions were graded as normal (no atherosclerosis), mild (1%–49% stenosis), moderate (50%–69% stenosis), severe (70%–99%) or totally occluded (100%) in epicardial coronary arteries of ≥2 mm in diameter. Coronary lesions with ≥50% luminal stenosis severity were defined as obstructive.

Per-vessel obstructive CAD was defined by ≥50% stenosis (including CTO) in 0, 1, 2 or 3 coronary artery vessels. For the purpose of classification for per-vessel analyses, we included four arterial territories: left main artery, left anterior descending artery, left circumflex artery and right coronary artery. The diagonal branches and obtuse marginal branches were considered as part of the left anterior descending artery and left circumflex artery system, respectively, whereas the posterolateral branches and posterior descending artery were considered as part of the right coronary artery or left circumflex artery system, depending on the coronary artery dominance.[19] Additionally, the proximal segments were defined as follows: left main, proximal and mid left anterior descending artery; proximal left circumflex artery and first obtuse marginal branch; and proximal and mid right coronary artery.[18] Per-patient obstructive CAD was defined by the maximal stenosis in ≥1 coronary vessel at the 50% stenosis threshold. Given that severe CAD (≥70% stenosis) is mainly associated with coronary ischaemia, and the need for coronary revascularisation, subanalyses were performed for patients with at least one coronary stenosis at the ≥70% luminal narrowing threshold to investigate CTO treatment allocation.

CTO was defined as complete interruption of the contrast-enhanced lumen of the coronary artery with recurrence of luminal opacification distal to the occlusion site as assessed by multiplanar reconstructions by CCTA.[20 21] The prevalence of CTO was determined using two denominators: (1) all patients undergoing CCTA and (2) patients with obstructive CAD.

Study outcomes

The primary endpoint was prevalent CTO as determined by CCTA. In patients with follow-up for early coronary revascularisation, a secondary endpoint of target vessel coronary revascularisation performed within 90 days after the time of CCTA was assessed.[22]

Statistical methods

Categorical variables were presented as counts with proportions and were assessed using Pearson's χ^2 or Fisher's exact test for cell counts <6. Continuous variables were presented as mean ±SD when normally distributed or median with IQR when non-normally distributed, and analysed using Student's unpaired t test or Mann–Whitney U test, as appropriate. The variables with significant missing values (>15%) were noted. Pairwise comparisons of plaque morphology were obtained using one-sample t tests, and were adjusted to account for multiple comparisons (ie, three pairwise comparisons) using the Bonferroni method. Clinical variables known or suspected to be associated with the presence of CTO or post-test revascularisation strategies were assessed using univariable and multivariable hierarchical mixed-effects logistic regression modelling, with hospital sites considered random effects, reporting ORs with 95% CIs. For this reason, we made the following assumptions: random effects follow a Gaussian distribution, the conditional distribution of the response is assumed to be Bernoulli with probability of success determined by cumulative distribution function, and the log-likelihood is approximated by adaptive Gaussian quadrature.[23] Statistical significance was accepted for two-tailed p values <0.05. All calculations were performed using STATA V.12.1 (Stata, College Station, Texas, USA).

RESULTS

Prevalence of CTO

Of a total of 27 125 screened adult patients, we excluded patients with known CAD (n=2350), congenital heart disease (n=111) and patients for whom clinical data regarding age, gender or CAD severity were lacking (n=919), resulting in a final study sample of 23 745 individuals. The prevalence of CTO for the entire study cohort (definition 1) was 1.4% (342/23 745). In patients with obstructive CAD (≥50% stenosis threshold), the prevalence of CTO was 6.2% (342/5559).

Clinical and angiographic characteristics of CTO

Demographic characteristics according to the presence or absence of CTO by CCTA are reported in table 1. The majority of individuals with CTO presented with a low-to-intermediate probability of obstructive CAD. Approximately two-thirds of the study sample presenting with CTO were symptomatic, with the most common presentation of atypical angina, followed by typical angina and non-cardiac chest pain. Mean age was higher for patients with CTO, with a higher prevalence of male sex and CAD risk factors with the exception of family history of premature CAD. In patients with LVEF data availability (33% of the study cohort), the majority of individuals with CTO exhibited normal LVEF, although LVEF was significantly lower among patients with CTO.

Prevalence of significant CAD among patients with CTO was equally distributed into one-vessel (33%), two-vessel (31.9%) and three-vessel or left-main CAD (35.1%). In total, 380 vessels (172 right coronary arteries, 114 left anterior descending arteries, 94 left circumflex arteries) were totally occluded, with the majority of individuals with single-vessel CTO (89.2%), followed by patients with two-vessel CTO (10.5%) and three-vessel CTO (0.3%), respectively. The most common CTO was the right coronary artery identified in 50.3% of patients with CTO, with 33.3% and 27.4% of individuals manifesting left anterior descending and left circumflex artery CTO, respectively. The location of CTO was in the proximal portion of the coronary arteries in the majority (57.1%) of cases (distribution of

Table 1 Baseline characteristics of the study population (n=23 745)

	Chronic total occlusion		
	No (n=23 403)	Yes (n=342)	p Value
Age, years	57.2±12.6	64.7±10.8	<0.0001
Male	12 671 (54.1)	255 (74.6)	<0.001
Hypertension	11 385 (49.1)	227 (67.2)	<0.001
Hyperlipidaemia	12 566 (54.1)	226 (66.9)	<0.001
Diabetes	3359 (14.4)	80 (23.7)	<0.001
Family history of premature CAD	8476 (36.8)	124 (36.9)	0.96
Current smoker	4144 (17.8)	94 (27.8)	<0.001
BMI, kg/m^2*	27.3±5.2	27.7±4.6	0.04
LVEF, %†	61.8±11.4	57.2±15.4	0.0009
Normal LVEF, >50%	6551 (85.3)	124 (70.5)	<0.001
Moderate LVEF, >30% ≤50%	968 (12.6)	38 (21.6)	<0.001
Low LVEF, ≤30%	161 (2.1)	14 (8.0)	<0.001
Pretest probability of obstructive CAD	34.6±29.1	41.9±33.5	<0.0001
Low	8970 (43.7)	141 (42.6)	0.68
Intermediate	9520 (46.4)	121 (36.6)	<0.001
High	2021 (9.9)	69 (20.9)	<0.001
Chest pain			
Asymptomatic	6886 (33.6)	135 (40.8)	0.006
Non-cardiac	2333 (11.4)	38 (11.5)	0.95
Atypical angina	8235 (40.2)	84 (25.4)	<0.001
Typical angina	3057 (14.9)	74 (22.4)	<0.001
CCTA results (no. of vessels with ≥50% stenosis, including CTO)			
Normal	10 097 (43.1)	0	<0.001
Non-obstructive	8089 (34.6)	0	<0.001
One-vessel disease	2984 (12.8)	113 (33.0)	<0.001
Two-vessel disease	1228 (5.3)	109 (31.9)	<0.001
Three-vessel disease or left main	1005 (4.3)	120 (35.1)	<0.001

Values are mean±SD or n (%).
*BMI available in 78% of the cohort.
†LVEF available in 33% of the cohort.
BMI, body mass index; CAD, coronary artery disease; CCTA, coronary CT angiography; CTO, chronic total occlusion; LVEF, left ventricular ejection fraction.

Table 2 Location and plaque morphology of chronic total occlusion

	No. of occluded segments (%)	Plaque composition (%)		
		Calcified	Partially calcified	Non-calcified
Left main	0			
LAD				
Proximal	29 (8.5)	25.2±30.8	54.8±33.0*	20.0±24.3†
Medial	50 (14.6)	29.3±36.8	47.7±35.5*	22.9±30.8†
Distal	26 (7.6)	13.4±19.5‡	49.5±28.5*	37.1±31.8
Diagonal artery 1	29 (8.5)	32.5±38.5	49.6±37.6	17.9±26.4†
Diagonal artery 2	10 (2.9)	21.7±24.3	54.2±29.9*	24.1±38.2
LCX				
Proximal	17 (5.0)	13.5±18.4	55.4±33.7*	31.1±35.3
Distal	47 (13.7)	26.9±28.5	52.6±33.8*	20.5±28.6†
Obtuse marginal 1	33 (9.7)	24.5±32.5	56.3±33.2*	19.2±25.0†
Obtuse marginal 2	13 (3.8)	17.5±16.9	62.2±25.5*	20.3±21.7†
Left posterolateral artery	0			
RCA				
Proximal	61 (17.8)	24.1±26.8	52.6±29.5*	23.3±27.2†
Medial	111 (32.5)	26.3±28.9	54.0±30.6*	19.7±25.7†
Distal	63 (18.4)	23.0±27.2	58.8±32.1*	18.1±25.4†
Right posterolateral artery	13 (3.8)	44.9±35.7‡	46.2±35.8	8.9±20.0†
Posterior descending artery	25 (7.3)	41.2±38.3‡	46.6±40.1	12.2±26.0†

Values are mean±SD or n (%).
*Significant differences between CP versus PCP.
†Significant differences between PCP versus NCP.
‡Significant differences between CP versus NCP.
CP, calcified plaque; LAD, left anterior descending artery; LCX, left circumflex artery; NCP, non-calcified plaque; PCP, partially calcified plaque; RCA, right coronary artery.

proximal occlusion per vessel: right coronary artery 63%; left anterior descending artery 54.9%; left circumflex artery 45.5%), with most CTOs being calcified or partially calcified (table 2).

Predictors of CTO

Multivariable mixed-effects logistic regression analyses revealed CTO to be associated with male sex, current smoking status, diabetes, typical angina, hypertension, family history of premature CAD and age. Conversely, the odds of prevalent CTO were reduced on the background of normal LVEF (table 3).

Early treatment strategies

Follow-up for early coronary revascularisation was available in 15 163 of the study sample, of which CTO was prevalent in 281 (1.9%) patients. Most patients with CTO (61%) were treated by medical therapy, while approximately one-third (39%) underwent early coronary revascularisation by surgical or percutaneous methods. In the subgroup of 1372 patients presenting with at least one severe coronary stenosis (≥70%), those with CTO were referred more often to coronary artery bypass grafting in lieu of lower rates of percutaneous coronary intervention as compared with patients without CTO (figure 1).

Table 3 Univariable and multivariable mixed-effects regression analyses for prediction of chronic total occlusion (n=23 745)

	Univariable			Multivariable		
	OR	95% CI	p Value	OR	95% CI	p Value
Age, years	1.05	1.04 to 1.06	<0.001	1.06	1.05 to 1.07	<0.001
Male	2.46	1.92 to 3.14	<0.001	3.12	2.39 to 4.08	<0.001
Hypertension	1.96	1.56 to 2.47	<0.001	1.47	1.14 to 1.88	0.003
Hyperlipidaemia	1.70	1.35 to 2.14	<0.001	1.20	0.94 to 1.53	0.14
Diabetes	2.10	1.63 to 2.72	<0.001	1.60	1.22 to 2.11	0.001
Family history of premature CAD	1.05	0.83 to 1.33	0.66	1.30	1.01 to 1.67	0.04
Current smoker	1.77	1.38 to 2.26	<0.001	2.02	1.55 to 2.64	<0.001
BMI, kg/m^2	1.01	0.99 to 1.03	0.25	1.01	0.98 to 1.03	0.58
Chest pain						
Asymptomatic	1.00			1.00		
Non-cardiac	0.77	0.52 to 1.12	0.17	0.93	0.63 to 1.39	0.73
Atypical angina	0.67	0.50 to 0.88	0.005	0.82	0.61 to 1.10	0.19
Typical angina	1.45	1.09 to 1.95	0.01	1.51	1.12 to 2.06	0.008
Pretest probability of obstructive CAD per 10%	1.10	1.06 to 1.13	<0.001	1.15	0.91 to 1.46	0.24
LVEF (%)*	0.96	0.95 to 0.97	<0.001	0.96	0.95 to 0.98	<0.001

*LVEF was used as a continuous variable.
BMI, body mass index; CAD, coronary artery disease; LVEF, left ventricular ejection fraction.

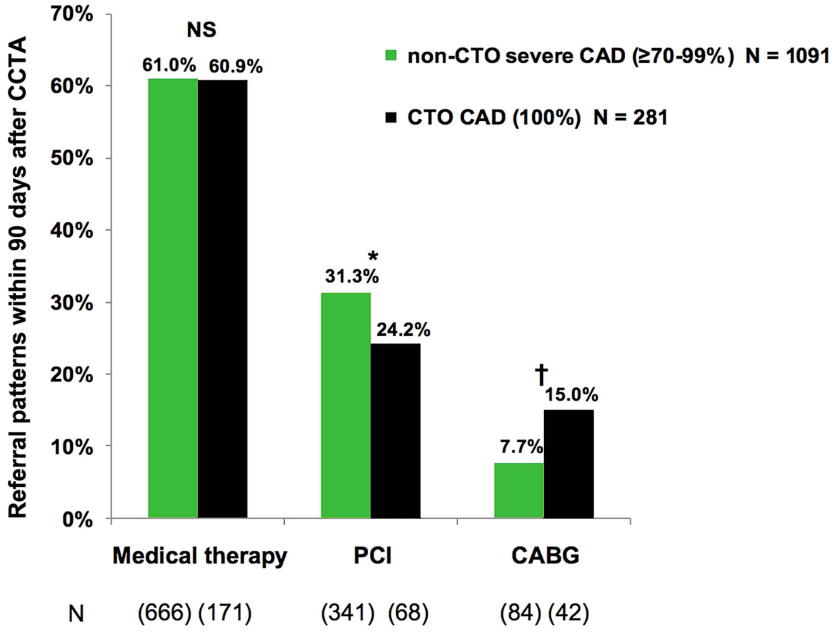

Figure 1 Early referral patterns (within 90 days after CT angiography) of patients with severe CAD (≥70%) with and without CTO (n=1372). Values are n (%). *p=0.02. †p<0.001. CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCTA, coronary CT angiography; CTO, chronic total occlusion; NS, non-significant; PCI, percutaneous coronary intervention.

Early referral patterns stratified by the presence of coronary vessel disease showed that surgical revascularisation was most often attempted in the subgroup of patients with CTO with three-vessel or left-main CAD, whereas percutaneous coronary revascularisation was most often chosen in subjects without CTO, but with one-vessel disease (table 4). By multivariable mixed-effects logistic regression analysis, early revascularisation by percutaneous coronary intervention among patients with ≥1 severe coronary stenosis (≥70%) was related to typical angina (OR 1.94, 95% CI 1.36 to 2.76, p<0.001), atypical angina (OR 1.66, 95% CI 1.21 to 2.29, p=0.002), age (OR 0.98, 95% CI 0.97 to 0.99, p=0.001) and hypertension (OR 0.76, 95% CI 0.58 to 1.00, p=0.048), and was not associated with the presence of CTO (OR 0.96, 95% CI 0.68 to 1.35, p=0.83). Conversely, the presence of CTO (OR 3.41, 95% CI 2.06 to 5.66, p<0.001) was the strongest independent predictor for early revascularisation by coronary artery bypass grafting among patients with ≥1 severe coronary stenosis (≥70%), followed by multivessel or left main obstructive CAD (OR 3.09, 95% CI 1.87 to 5.12, p<0.001), atypical angina (OR 1.71, 95% CI 1.01 to 2.92, p=0.047), current smoking status (OR 1.69, 95% CI 1.06 to 2.68, p=0.027) and hyperlipidaemia (OR 1.68, 95% CI 1.03 to 2.74, p=0.036). Patients with CTO referred to percutaneous coronary intervention (n=68) versus coronary artery bypass grafting (n=42) differed for the extent of obstructive CAD, LV systolic function and hyperlipidaemia (table 5).

Table 4 Early referral patterns of patients with severe CAD (≥70%) with and without CTO stratified by the presence of coronary vessel disease on CCTA (n=1372)

	Chronic total occlusion		
	No (n=1091)	Yes (n=281)	p Value
Early medical therapy			
One-vessel disease	323 (64.0)	68 (78.2)	0.01
Two-vessel disease	207 (62.4)	56 (62.2)	0.98
Three-vessel disease or left main	136 (53.5)	47 (45.2)	0.15
Early PCI			
One-vessel disease	167 (33.1)	18 (20.7)	0.02
Two-vessel disease	101 (30.4)	24 (26.7)	0.49
Three-vessel disease or left main	73 (28.7)	26 (25.0)	0.47
Early CABG			
One-vessel disease	15 (3.0)	1 (1.2)	0.49
Two-vessel disease	24 (7.2)	10 (11.1)	0.23
Three-vessel disease or left main	45 (17.7)	31 (29.8)	0.01

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCTA, coronary CT angiography; CTO, chronic total occlusion; PCI, percutaneous coronary intervention.

DISCUSSION

In a prospective contemporary multinational registry of consecutive individuals undergoing CCTA, this present study set out to determine the prevalence, characteristics and clinical management of CTO among patients without prior known CAD. We observed the prevalence of CTO to be low, but significantly increased in the presence of obstructive CAD. Presence of CTO by CCTA was associated with male sex, current smoking, diabetes, hypertension, family history of CAD, age and angina presentation. The majority of patients with CTO were symptomatic and yet demonstrated well-preserved LV systolic function, with referral to coronary revascularisation in approximately one-third of patients. Notably, the findings from this study may be considered widely generalisable given the high number of enrolled subjects and inclusion of multiple clinical sites in North America, Europe and Asia.

To date, the prevalence of CTO has been assessed only in higher risk patients undergoing invasive coronary angiography.[7–10] Prior studies have demonstrated frequencies of CTO ranging from 35% to 52% among patients with obstructive CAD.[7 9] More recently, in a prospective three-centre coronary angiography registry,[10] CTOs were discovered in 18.4% of patients with obstructive CAD. The disparity in the frequency of CTO between the current findings and prior angiographic reports is unsurprising given the generally lower risk presentation of CCTA population. Interestingly, the majority of individuals with CTO in our cohort presented with a low-to-intermediate rather than high probability of obstructive CAD. This study offers information incremental to that of

Table 5 Clinical presentation of patients with CTO referred to PCI versus CABG for early coronary revascularisation (n=110)

	Early PCI (n=68)	Early CABG (n=42)	p Value
Age, years	63.8±10.9	65.2±8.7	0.55
Male	46 (67.7)	33 (78.6)	0.22
Hypertension	44 (65.7)	21 (51.2)	0.14
Hyperlipidaemia	42 (63.6)	35 (85.4)	0.02
Diabetes	15 (22.1)	10 (24.4)	0.78
Family history of premature CAD	24 (36.4)	14 (34.2)	0.82
Current smoker	20 (29.4)	10 (24.4)	0.57
BMI, kg/m^2	27.7±3.9	27.6±3.9	0.69
LVEF, %*	59.4±12.1	52.2±14.1	0.03
Pretest probability of obstructive CAD	48.5±33.5	53.4±33.3	0.37
Low	21 (31.3)	10 (26.3)	0.59
Intermediate	29 (43.3)	16 (42.1)	0.91
High	17 (25.4)	12 (31.6)	0.49
Chest pain			
Asymptomatic	18 (26.9)	10 (26.3)	0.95
Non-cardiac	7 (10.5)	5 (13.2)	0.75
Atypical angina	25 (37.3)	10 (26.3)	0.25
Typical angina	17 (25.4)	13 (34.2)	0.34
CCTA results (no. of vessels with ≥50% stenosis, including CTO)			
One-vessel disease	18 (26.5)	1 (2.4)	0.001
Two-vessel disease	24 (35.3)	10 (23.8)	0.21
Three-vessel disease or left main	26 (38.2)	31 (73.8)	<0.001

*LVEF available only in 42% of the CTO group.
BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCTA, coronary CT angiography; CTO, chronic total occlusion; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

invasive angiographic observations on CTO occurrence, and extends the understanding of CTO prevalence in patients with a lower likelihood presentation undergoing non-invasive angiography.

To date, few studies have assessed the angiographic characteristics of CTO in an unselected patient population. From data developed through the 1997–1999 National Heart, Lung and Blood Institute Dynamic Registry, CTOs were observed to be most prevalent in the right coronary artery and least common in the left circumflex artery.[24] Similar results were encountered in the prospective study of Fefer *et al*[10] who identified the right coronary artery as the site of CTO in the majority of cases. These findings are in accordance with our present data confirming the highest prevalence of CTO within the right coronary artery region. Interestingly, we observed an equal distribution of one-vessel, two-vessel and three-vessel or left main obstructive disease among patients with CTO. Further, the majority of CTO lesions showed calcified or partially calcified plaque morphologies. Provided that the extent and severity of calcification increase with occlusion duration,[25] this observation may be interpreted as indirect evidence for the predominance of older CTO in our cohort. These findings may offer clues as to the pathogenesis of CTO, and large-scale longitudinal studies assessing plaque composition and other atherosclerotic plaque features among individuals at risk of CTO development now appear warranted.

In a single-centre registry of 8004 patients undergoing invasive coronary angiography, Christofferson *et al*[9] linked peripheral vascular disease, smoking and hypertension to the presence of CTO. Other angiographic studies either found increasing age or prior myocardial infarction to be positively associated with CTO.[24 26] In lieu of these findings, the current investigation may be considered the first to report on clinical predictors and symptomatic status of unselected patients with CTO undergoing CCTA. Interestingly, while expectedly advancing age, male sex, current smoking, diabetes, hypertension, family history of premature CAD and typical angina conferred higher risk for CTO, we noted a strong relationship between increasing LVEF and attenuation of risk of CTO. The present findings are in line with prior pioneer studies emphasising the increasing prevalence, severity and extent of CAD in patients with a higher burden of main cardiovascular risk factors.[13 27] Yet, the present study findings examining individuals with lower pretest probability of obstructive CAD observed a non-negligible rate of CTOs, and emphasise the importance of integration of CAD risk factors and symptom presentation to forecast the presence of CTO. To this end, the present data underline the need to develop a future predictive model for identifying the presence of CTO in lower risk populations, including asymptomatic subjects.

There are scant data about the practicing trends regarding referral patterns and management for a CTO population. Mostly, patients undergoing coronary revascularisation for CTO have stable or progressive angina with preserved LV function and/or documented ischaemia.[28 29] In the present study, merely 39.1% of subjects with CTO were referred for early coronary revascularisation despite most CTO individuals presenting with symptoms consistent with angina and normal LV function. Whether these individuals will derive clinical benefit from CTO revascularisation remains to be determined. By relevance, the presence of CTO was related to significantly higher surgical revascularisation rates and lower percutaneous revascularisation rates when compared with individuals presenting with severe CAD, but without CTO. Further, in the current study, CTO was the strongest predictor for coronary artery bypass grafting, but was unrelated to the use of percutaneous coronary intervention. This finding contrasts with a prior registry analysis employing invasive catheterisation in which CTO was the strongest predictor against percutaneous coronary intervention with no significant impact on the referral patterns for coronary artery bypass grafting.[9] Instead, the rates of coronary revascularisation by either percutaneous coronary intervention or coronary artery bypass grafting observed in the current study corresponded well with findings of a more recent prospective angiography registry.[10] The disparity between our and prior angiographic studies with regard to early management of patients with CTO may be temporally influenced, or may represent a function of differing pretest probability presentations as well as wide variability between percutaneous coronary intervention centres in successful revascularisation of CTO. Not surprisingly, patients referred for coronary artery bypass grafting presented with more extensive CAD, including left main involvement, and worse LV systolic function than patients referred for percutaneous coronary intervention. This finding may, in part, explain the stronger association between the presence of CTO and early revascularisation by coronary artery bypass grafting than percutaneous coronary intervention.

This study is not without limitations. This was an observational multicentre registry with variable pretest probability of CAD for individuals at different sites. Yet, the results of this study regarding the prevalence and significance of CTO among patients referred for CCTA were based on the largest currently available pooled patient cohort, and may serve to generate hypotheses for the design of future trials. The adopted definition of CTO did not account for the estimated time of occlusion prior to non-invasive angiographic interrogation, which

may have influenced the perceived rate of revascularisation of occluded vessels in our cohort. Based on a previous histopathology study,[25] however, the predominance of calcified and partially calcified CTO morphology are in accordance with observations in the present study, and may offer clues as to the approach of CTOs once identified by CCTA. CTO was defined by CCTA and not coronary angiography; therefore, the possibility of false-positive and false-negative CCTA findings may exist. Finally, the reported referral patterns of patients with CTO to percutaneous coronary intervention or coronary artery bypass grafting were not governed by standard criteria, but rather clinician discretion. Thus, the possibility of selection bias that is present in all observational studies cannot be discounted.

CONCLUSIONS

The present study represents the first data to determine the prevalence, characteristics and treatment strategies of CTO among patients undergoing non-invasive angiography for suspected CAD in a contemporary clinical setting; and demonstrates a low, but non-negligible, rate of CTO that is more prevalent in individuals with obstructive CAD and low-to-intermediate probability of obstructive CAD. The presence of CCTA-identified CTO was strongly associated with age, gender, angina status and CAD risk factors. Despite the presence of symptoms and preserved LVEF, the majority of patients with CTO were managed medically, with CTO a stronger predictor of surgical rather than percutaneous revascularisation.

Key messages

What is already known on this subject?
While coronary CT angiography (CCTA) has been successfully employed in the planning of chronic total occlusion (CTO) revascularisation, data describing the prevalence, characteristics and management of CTO in patients undergoing CCTA for suspected coronary artery disease (CAD) have not been reported.

What might this study add?
The present study demonstrates that: (1) CTO are not uncommon in a contemporary CCTA population, and are more prevalent in individuals with obstructive CAD; (2) the presence of CTO is strongly associated with age, gender, angina status and CAD risk factors and (3) despite the presence of symptoms, the majority of patients with CCTA-identified CTO were managed medically, with CTO being a stronger predictor of surgical rather than percutaneous revascularisation.

How might this impact on clinical practice?
This study offers information incremental to developing a future predictive model for identifying the presence of CTO in patients undergoing non-invasive CCTA, and indicates the need for defining the most optimal treatment strategies of CTO in a contemporary CCTA population.

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Current trends in patients with chronic total occlusions undergoing coronary CT angiography

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