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General practice preventive health care in non-obstructive coronary artery disease determined by coronary computed tomography angiography

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ABSTRACT

Background: The aim of this study was to compare changes in health service utilization, preventive medical management, and cholesterol levels in patients without coronary artery disease (CAD) or with non-obstructive CAD as determined by coronary computed tomography angiography (CTA).
Methods: Single-center five-year observational registry-based cohort study of consecutive patients with chest pain undergoing coronary CTA with subsequent 12 months follow-up in general practice.
Results: We included 3032 patients with a normal test result (n = 2179) or a diagnosis of non-obstructive CAD (n = 853) by coronary CTA. Median age was 55 (interquartile range: 47–63) years and 44% were males. After coronary CTA, the probability of a decrease in consultations with general practitioner was higher in patients with no CAD compared to patients with non-obstructive CAD (adjusted OR = 0.81 [95% CI: 0.68–0.96], $P = 0.016$). Accordingly, patients with non-obstructive CAD more frequently received prescriptions on lipid-lowering medical therapy (adjusted OR = 4.50 [95% CI: 3.31–6.12], $P < 0.001$) than patients with no CAD after coronary CTA. In patients with non-obstructive CAD, mean total-cholesterol reduction was 0.51 ($P < 0.001$) compared to 0.13 mmol/L ($P < 0.001$) in patients without non-obstructive CAD. The relative reduction in low-density lipoprotein was 14% higher ($P < 0.001$) in patients with compared to patients without non-obstructive CAD after coronary CTA.
Conclusions: Coronary CTA with subsequent follow-up in general practice has the potential to align health service utilization that prioritizes high-risk patients and facilitate optimized preventive management.

1. Introduction

Coronary computed tomography angiography (CTA) is used increasingly as a non-invasive strategy for patients suspected of coronary artery disease (CAD) [1,2]. By design, coronary CTA identifies a larger spectrum of disease than non-invasive functional testing because patients with non-obstructive CAD are identified. Approximately, 30% of patients with chest pain and low to intermediate probability of CAD referred to coronary CTA have non-obstructive CAD [1]. Patients with non-obstructive CAD have a higher risk of subsequent cardiac events and mortality than those with no CAD [1,3]. Moreover, meta-analyses have shown that statins and aspirin in patients with non-obstructive CAD are associated with improved clinical outcomes [4,5].

Optimally, the diagnosis of non-obstructive CAD should translate into appropriate preventive management and health service allocation. However, patients with non-obstructive CAD determined by coronary CTA have only been identified within the recent decade; hence recommendations for optimal preventive management have not yet been specified [6,7]. Whereas patients with obstructive CAD often undergo additional in-hospital testing and interventional treatment, follow-up of the large proportion of patients with non-obstructive CAD most often takes place in general practice [8]. Information on the influence of having non-obstructive CAD on the downstream preventive health care and cholesterol levels in general practice is sparse. The aim of this study was to compare changes in health service utilization, preventive medical management, and cholesterol levels in patients either without CAD or with non-obstructive CAD as determined by coronary CTA.

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2. Material and methods

We performed a five-year observational registry-based cohort study of consecutive patients with chest pain undergoing coronary CTA at Aarhus University Hospital, Central Denmark Region, Denmark, from 1 January 2009 to 31 December 2013. Patients were referred by their general practitioner (GP) to cardiac evaluation and subsequently underwent diagnostic testing with coronary CTA. In our institution, the preferred initial diagnostic modality in patients with first-time chest paint and with no known CAD and low to intermediate pre-test risk is coronary CTA [9]. Patients >18 years old with symptoms indicative of stable CAD were included. Exclusion criteria were residency outside the Central Denmark Region at any time during 12 months before to 12 months after the coronary CTA, pregnancy, known CAD (previous myocardial infarction, percutaneous coronary intervention, or bypass surgery), and congestive heart failure. Moreover, patients were excluded in the event of obstructive CAD at coronary CTA or referral for further diagnostic testing following coronary CTA.

The Danish Data Protection Agency (J.no. 1-16-02-236-15) and the Danish Patient Safety Authority (J.no. 1-16-02-236-15) approved the study. According to Danish law, this study does not require ethical approval.

2.1. Data sources and definitions

Data from the most recent CTA procedure (defining the index date reported in the Western Denmark Heart Registry (WDHR) [10]) were collected and linked to data from other Danish registries [11] using the 10-digit Danish Civil Registration number (CPR number). Chest pain was categorized as typical angina, atypical angina (including dyspnea), or unspecific chest pain and the updated Diamond-Forester risk score was calculated [12]. Information about hypertension, diabetes mellitus, and hypercholesterolemia was obtained from the Danish National Patient Registry [13], whereas data on total-cholesterol, low-density lipoprotein (LDL) cholesterol, and glycated hemoglobin (HbA1c) was obtained from the Clinical Laboratory Information Registry [14]. Hypertension was defined by diagnosis or systolic blood pressure ≥ 180 mm Hg or diastolic blood pressure ≥ 110 mm Hg; diabetes mellitus by diagnosis or HbA1c ≥ 48 mmol/mol; hypercholesterolemia by a diagnosis of familial hypercholesterolemia or total-cholesterol ≥ 8 mmol/L, or LDL-cholesterol ≥ 6 mmol/L. Based on guidelines for primary cardiovascular prevention, we defined high-estimated cardiovascular risk as the presence of hypertension and/or diabetes mellitus and/or hypercholesterolemia [15,16]. We assessed the burden of comorbidity by the Charlson Comorbidity Index (CCI) and all diagnoses registered in the Danish National Patient Registry in the 10-year period before the index date [13,17]. The CCI score was categorized as low (CCI score: 0), moderate (CCI score: 1–2), or severe (CCI score: ≥3) [17]. From the Aarhus University Prescription Database, we obtained data on redeemed lipid-lowering, anti-hypertensive, anti-diabetic medical therapy (Appendix Table A1) [18,19]. Information about in-hospital activity was obtained from the Danish National Patient Registry [13] and information on activity in general practice was obtained from the Danish National Health Service Registry [20].

2.2. Coronary CTA

Coronary CTA was performed according to guidelines [21] using either a 64-slice SOMATOM Sensation or Definition Flash CT-scanner (Siemens, Forchheim, Germany) as previously described [1]. In short, an initial non-contrast scan was performed for quantitation of coronary calcium by the Agatston score [22]. Coronary CTA was performed using 80–120 kV tube voltage, dose-reduction strategies, and 70 mL of contrast unless contraindicated (allergy to contrast, or renal insufficiency). All patients received 0.8 mg sublingual nitrates and oral/intravenous beta-blockers or ivabradine targeting a heart rate < 60 beats/min. The coronary CTA results were classified as no CAD (0% luminal stenosis and Agatston score = 0), non-obstructive CAD (1–49% luminal stenosis), or obstructive CAD (≥50% luminal stenosis) [1].

2.3. Outcomes and follow-up

Study outcomes were changes in medical therapy, in-hospital and GP activities, as well as total and LDL plasma-cholesterol and HbA1c concentrations 12 months after coronary CTA compared to 12 months before coronary CTA.

2.3.1. In-hospital and general practice activities

In-hospital activity was defined as cardiovascular admissions and outpatient consultations within 12 months before and 12 months after the index date. We included face-to-face contact activities in general practice as consultations with GPs within 12 months before to 12 months after the index date. A difference in the sum of activity 12 months before the index date compared to >7 days < 12 months after was defined as: "no changes in consultations/admissions after coronary CTA" if difference = 0; "decrease in consultations/admissions after coronary CTA" if difference < 0; "increase in consultations/admissions after coronary CTA" if difference > 0. Because the majority of patients were frequently scheduled for an outpatient hospital or GP consultation to receive oral information about the study result, a deferral period of 7 days after coronary CTA was applied to exclude cardiovascular testing initiated as part of the cardiac evaluation.

2.3.2. Medical therapy

Information about defined daily dose (DDD) for each ATC code [18,19] was obtained 12 months before to 12 months after the index date giving a maximum sum of 365 DDDs in each period. Use of medical therapy was defined as ≥1 DDDs. Differences <5% in DDDs 12 months before the index date compared to 12 months after were categorized as "no change after coronary CTA". In patients with no prescriptions (DDDs = 0) of medical therapy 12 months before coronary CTA, differences ≥5% in DDDs compared to 12 months after the index date were categorized as "initiation after coronary CTA". In patients with prescriptions of medical therapy 12 months before coronary CTA, differences ≥5% in DDDs compared to 12 months after the index date were categorized as "intensification after coronary CTA" [23].

2.3.3. Blood samples

The most recently available blood sample 12 months before coronary CTA was compared with the most recently available equivalent blood sample ≥1 month < 12 months after coronary CTA. Measurements obtained at least 1 month after coronary CTA were used to allow time for post-test changes to occur [24,25].

3. Statistical analysis

Categorical variables are reported as proportions and presented as numbers with corresponding percentages (%). Continuous variables are presented as medians (interquartile range [IQR]; range) or means (with standard deviation [SD] and/or 95% confidence intervals [CI]). Chi-squared test, paired *t*-test, *t*-test, or Mann-Whitney test were used for comparisons. We categorized changes after coronary CTA in medical therapy, consultation with GPs, and in-hospital cardiovascular admission and outpatient consultation as "no change after coronary CTA", "decrease after coronary CTA", or "increase after coronary CTA" and used this variable as dependent variable in logistic regression comparing patient with no CAD to patients with non-obstructive CAD. Odds ratios (ORs) are presented with 95% CIs and in multivariable logistic regression adjustments were done for age, male gender, high-estimated cardiovascular risk, and CCI score.

In a sensitivity analysis, we included health service utilization 7 days post coronary CTA, and compared consultations with GPs, and in-hospital cardiovascular admissions and outpatient consultations 12 months before the index date to 12 months after.

Overall, we performed complete-case analysis on available data. Statistical analyses were performed using SAS (Version 9.4. SAS Institute. Cary, NC, USA).

4. Results

The total study cohort consisted of 3032 patients discharged to their GP with a normal test result (n = 2179) or a diagnosis of non-obstructive CAD (n = 853) as determined by coronary CTA (Appendix Fig. B1). No patients were lost to follow-up. Baseline characteristics are presented in Table 1. Median (IQR; range) age was 55 (47–63; 18–90) years and 1329 (44%) were males. A diagnosis of non-obstructive CAD was associated with higher age, male gender, higher cardiovascular risk profile, and increased co-morbidity. Coronary CTA acquisition characteristics are presented in Appendix Table A2.

4.1. Health service utilization

Overall, the number of consultations with GPs decreased following coronary CTA among all patients (Appendix Table A3). Similarly, the overall number of in-hospital cardiovascular admissions was also lower after than before coronary CTA, but the decrease reflected that the number of in-hospital cardiovascular outpatient consultations only decreased in patients with no CAD. The frequency of a decrease in consultations with GPs after coronary CTA was highest in patients with no CAD compared to patients with non-obstructive CAD. The association between the coronary CTA result and changes in health service utilization is shown in Table 2. As expected, the sensitivity analysis including health service utilization within the deferral period of 7 days after coronary CTA changed the result by showing an increased activity related to this specific period (Appendix Tables A4 and A5). A total of 53% patients with non-obstructive CAD and 48% patients with no CAD experienced an increase in in-

hospital cardiovascular outpatient consultations after coronary CTA related to this period (Appendix Table A5).

4.2. Prescriptions of medical therapy

Overall, the number of prescriptions including lipid-lowering, antihypertensive, and anti-diabetic medical therapies was higher after than before coronary CTA (Appendix Table A3). After coronary CTA, patients with non-obstructive CAD received prescriptions on lipid-lowering medical therapy or intensified prescription on lipid-lowering medical therapy more frequently than patients with no CAD (Table 2). During the entire study period, 41% of patients with non-obstructive CAD never received nor initiated any lipid-lowering therapy, while the proportion was higher (67%, $P < 0.001$ vs. non-obstructive CAD) in patients with no CAD. Similarly, antihypertensive medical therapy was less frequently absent or not initiated in patients with non-obstructive CAD than in patients with no CAD (38% vs. 56%, $P < 0.002$).

4.3. Blood sample measurements

Mean total plasma-cholesterol and LDL-cholesterol concentrations were lower after than before coronary CTA in both groups (Table 3). However, the relative reductions in cholesterol concentrations were most pronounced among patients with non-obstructive CAD (Fig. 1). The number of blood sample measurements for plasma cholesterol and HbA1c decreased following coronary CTA in both patients with no CAD or non-obstructive CAD (Table 3). The number of patients having plasma cholesterol measurements after coronary CTA was higher in patients with non-obstructive CAD than in patients with no CAD (Table 3).

5. Discussion

This study showed that the presence of non-obstructive CAD determined by coronary CTA in real-world practice was associated with the preventive management strategy and health service utilization during follow-up of patients at hospital and by GPs. In patients with non-obstructive CAD monitoring of plasma cholesterol and HbA1 concentrations was more intense than in patients with no CAD. Accordingly, a more pronounced absolute reduction in cholesterol levels in the former group was observed.

It has been demonstrated that coronary CTA testing affects patient and physician behaviour [26,27] and facilitates more appropriate use of statins and aspirin [28,29]. These changes in patient management have been linked to the improved clinical outcomes of coronary CTA compared to traditional non-invasive functional testing [30]. The findings indicate that the use of coronary CTA may translate into differentiated preventive management that aligns health service allocation more closely with a potential individual risk during subsequent follow-up by GPs [4,5]. Our results confirm previous observations of a strong impact of coronary CTA on prescription of preventive medical therapy and cholesterol levels [25,26,31,32]. The present study adds to these findings by including pre- and post-test data from the primary health care sector. Although our results do not allow a quantitation of the relative effect of outcomes from the GP, it is to our knowledge the first study to report a comprehensive analysis including data from both the primary and the secondary health care sector.

The present findings indicate that intensity of cholesterol measurements and prescribed preventive medical therapy after coronary CTA by GPs might be influenced by objective evidence of non-obstructive CAD

Table 1
Baseline characteristics.

	Total N = 3032	No CAD n = 2179		Non-obstructive CAD n = 853		*P* value
			Missing[a]		Missing[a]	
Male gender	1329 (43.8)	906 (41.6)	0 (0)	423 (49.6)	0 (0)	<0.001
Age years, median	55	52	0 (0)	61	0 (0)	<0.001
(IQR range)	(47–63; 18–90)	(44–60; 18–90)		(55–68; 19–85)		
Family history of CAD	1246 (41.1)	907 (41.6)	387 (17.8)	339 (39.7)	162 (19.0)	0.488
BMI ≥ 25 kg/m^2	1457 (48.1)	1030 (47.3)	380 (17.4)	427 (50.1)	151 (17.7)	0.104
Smoking	1436 (47.4)	979 (45.0)	429 (19.7)	457 (53.6)	166 (19.5)	<0.001
Hypertension	341 (11.3)	217 (10.0)	0 (0)	124 (14.5)	0 (0)	<0.001
Diabetes mellitus	173 (5.7)	96 (4.4)	0 (0)	77 (9.0)	0 (0)	<0.001
Hypercholesterolemia	59 (2.0)	37 (1.7)	0 (0)	22 (2.6)	0 (0)	0.114
High-estimated cardiovascular risk[b]	514 (17.0)	319 (14.6)	0 (0)	195 (22.9)	0 (0)	<0.001
Number of cardiovascular risk factors[c]						
1	456 (15.0)	289 (13.26)		167 (19.6)		<0.001
2	57 (1.9)	29 (1.3)		28 (3.3)		0.000
3	1 (0.0)	–		1 (0.1)		–
Charlson Co-morbidity Index score						
0 low	2289 (75.5)	1696 (77.8)	0 (0)	593 (69.5)	0 (0)	<0.001
1–2 moderate	638 (21.0)	420 (19.3)	0 (0)	218 (25.6)	0 (0)	
≥3 severe	105 (3.5)	63 (2.9)	0 (0)	42 (4.9)	0 (0)	
Symptoms			419 (19.2)		28 (3.3)	
Unspecific chest pain	166 (5.5)	90 (4.1)		76 (8.9)		<0.001
Atypical angina	1639 (54.1)	1093 (50.2)		546 (64.0)		
Typical angina	780 (25.7)	577 (26.5)		203 (23.8)		
Updated Diamond-Forester score %, median	23	20	419 (19.2)	31	28 (3.3)	<0.001
(IQR; range)	(14–37; 3–87)	(13–32; 3–86)		(20–46; 6–87)		
Intermediate (15%–85%) pre-test risk	1882 (62.1)	1161 (53.3)	419 (19.2)	721 (84.5)	28 (3.3)	<0.001
Pre-test risk (15%–50%)	1632 (53.8)	1074 (49.3)		558 (65.4)		<0.001
Pre-test risk > 50%	255 (8)	88 (4.0)		167 (19.6)		<0.001
Agatston score, median	0	0	363 (16.7)	35	9 (1.1)	<0.001
(IQR; range)	(0–7; 0–10,000)	(0–0; 0–0)		(1–105; 10–10,000)		
Serum creatinine, μmol/L, median	72	71	378 (17.4)	73	144 (16.9)	0.016
(IQR; range)	(62–82; 24–250)	(62–81; 24–185)		(63–84; 36–250)		

Values are n (%) if not stated otherwise.
CAD, coronary artery disease; BMI, body mass index; IQR, interquartile range.
[a] Missing data values in Western Denmark Heart Registry.
[b] Patients with hypertension, diabetes mellitus, or hypercholesterolemia.
[c] Number of cardiovascular risk factors in patients with high-estimated cardiovascular risk (hypertension, diabetes mellitus, or hypercholesterolemia).

Table 2
The association between result of the coronary CTA and changes in health service utilizations and in the prescriptions of medical therapy.

	No CAD n = 2179	Non-obstructive CAD n = 853	Odds ratio (95% CI)			
			Unadjusted	*P* value	Adjusted[a]	*P* value
Health service utilizations						
Consultations with general practitioner (%)						
No change after coronary CTA	263 (12.1)	112 (13.1)	1.10 (0.87–1.40)	0.425	1.14 (0.88–1.48)	0.321
Decrease after coronary CTA	1194 (54.8)	425 (49.8)	0.82 (0.70–0.96)	0.014	0.81 (0.68–0.96)	0.016
Increase after coronary CTA	722 (33.1)	316 (37.0)	1.19 (1.01–1.40)	0.041	1.19 (0.99–1.42)	0.062
Cardiovascular admissions (%)						
No change after coronary CTA	1654 (75.9)	605 (70.9)	0.77 (0.65–0.92)	0.005	0.92 (0.75–1.12)	0.394
Decrease after coronary CTA	385 (17.7)	158 (18.5)	1.06 (0.86–1.30)	0.581	0.99 (0.79–1.25)	0.958
Increase after coronary CTA	140 (6.4)	90 (10.6)	1.72 (1.30–2.27)	<0.001	1.22 (0.90–1.66)	0.190
Cardiovascular outpatient consultations (%)						
No change after coronary CTA	984 (45.2)	307 (36.0)	0.68 (0.58–0.80)	<0.001	0.68 (0.57–0.82)	<0.001
Decrease after coronary CTA	957 (43.9)	378 (44.3)	1.02 (0.87–1.19)	0.844	1.03 (0.87–1.23)	0.709
Increase after coronary CTA	238 (10.9)	168 (19.7)	2.00 (1.61–2.48)	<0.001	1.93 (1.52–2.45)	<0.001
Prescriptions of medical therapy						
Prescriptions in lipid-lowering medical therapy (%)						
No change after coronary CTA	110 (5.0)	91 (10.7)	2.25 (1.68–3.00)	<0.001	1.59 (1.15–2.18)	0.005
Initiation after coronary CTA	87 (4.0)	144 (16.9)	4.88 (3.69–6.46)	<0.001	4.50 (3.31–6.12)	<0.001
Intensification after coronary CTA	336 (15.4)	200 (23.4)	1.68 (1.38–2.04)	<0.001	1.25 (1.01–1.55)	0.043
Prescriptions in anti-hypertensive medical therapy (%)						
No change after coronary CTA	72 (3.3)	72 (8.4)	2.70 (1.93–3.78)	<0.001	1.74 (1.20–2.52)	0.003
Initiation after coronary CTA	91 (4.2)	52 (6.1)	1.49 (1.05–2.11)	0.026	1.66 (1.13–2.44)	0.010
Intensification after coronary CTA	606 (27.8)	332 (38.9)	1.65 (1.40–1.95)	<0.001	1.14 (0.95–1.38)	0.167
Prescriptions in anti-diabetic medical therapy (%)						
No change after coronary CTA	16 (0.7)	19 (2.2)	–	–	–	–
Initiation after coronary CTA	15 (0.7)	10 (1.2)	–	–	–	–
Intensification after coronary CTA	55 (2.5)	43 (5.0)	2.05 (1.36–3.08)	<0.001	1.51 (0.92–2.47)	0.103

CTA, computed tomography angiography; CAD, coronary artery disease; CI, confidence intervals.
[a] Logistic regression adjusted for age, male gender, high-estimated cardiovascular risk, and Charlson Co-morbidity Index score.

beyond a population-based cardiovascular risk calculation for primary prevention [33]. However, the influence of the coronary CTA results must be interpreted in the light of GPs' detailed knowledge of their patients, and thus individualised guidance on decision making of the preventive management strategy [15,16]. Nevertheless, the fact that over one third of patients with non-obstructive CAD had no follow-up, were not prescribed lipid-lowering therapy, or had any cholesterol measurements one year after coronary CTA may reflect an overall underuse of preventive therapy in such patients in general practice. Notably, the present study demonstrates that even in "healthy" patients with no CAD, prescriptions of preventive medical therapy by GPs were more likely after than before the coronary CTA test. This finding may be explained by increased patient and GP awareness on patient risk profiles, which otherwise would not have been addressed. Our findings of a heterogeneous treatment pattern for patients with non-obstructive CAD and an increased treatment of patients without CAD emphasizes the need of guidelines on the downstream management strategy in patients without obstructive CAD after coronary CTA testing, which should be based on outcome studies and analyses of cost-effectiveness.

In this study, almost 50% of the patients "ruled" out as having CAD subsequently had a cardiovascular hospital outpatient consultation within seven days after the coronary CTA test. This finding most likely reflects previously scheduled cardiovascular in-hospital health service allocation [34], which was not systematically cancelled as part of the imaging procedure, but also raises the question whether some of the cardiovascular outpatient consultations, indeed, are

Table 3
Plasma cholesterol and HbA1c concentrations.

	No CAD n = 2179					Non-obstructive CAD n = 853					Group difference	
	Before	After	n (%)[a]	Difference Δ^{No} (95% CI)	*P* value	Before	After	n (%)[a]	Difference Δ^{Non} (95% CI)	*P* value	$\Delta^{Non} - \Delta^{No}$ (95% CI)	*P* value
Measurements, n (%)												
Total-cholesterol	1879 (86.1)	930 (42.7)	854 (39.2)	–	<0.001	767 (89.9)	534 (62.6)	495 (58.0)	–	<0.001	–	<0.001
LDL-cholesterol	1791 (82.2)	904 (41.5)	804 (36.9)	–	<0.001	732 (85.8)	533 (62.5)	475 (55.7)	–	<0.001	–	<0.001
HbA1c	894 (41.0)	636 (29.2)	380 (17.4)	–	<0.001	486 (57.0)	408 (47.8)	288 (33.8)	–	<0.001	–	<0.001
Mean values (±SD)												
Total-cholesterol, mmol/L	5.15 (1.11)	5.02 (1.07)	–	−0.13 (−0.20 to −0.07)	<0.001	5.22 (1.07)	4.70 (1.06)	–	−0.51 (−0.61 to −0.41)	<0.001	−0.38 (−0.50 to −0.26)	<0.001
LDL-cholesterol, mmol/L	3.05 (0.99)	2.92 (0.97)	–	−0.13 (−0.19 to −0.07)	<0.001	3.09 (1.00)	2.66 (1.01)	–	−0.43 (−0.52 to −0.34)	<0.001	−0.30 (−0.41 to −0.19)	<0.001
HbA1c, mmol/mol	41.13 (9.91)	40.49 (9.11)	–	−0.63 (−1.12 to −0.15)	0.010	42.65 (11.09)	42.14 (10.44)	–	−0.51 (−1.38–0.37)	0.255	0.13 (−0.87–1.13)	0.802

Number (%) of patients with measurements (top) and mean (SD) values (bottom) for patients with measurements in both periods.
Differences in mean follow-up times in blood sample measurements before to after coronary CTA between patients with no CAD and non-obstructive CAD were not significant.
CAD, coronary artery disease; LDL, low-density lipoprotein; HbA1c, glycated hemoglobin; CI, confidence intervals; CTA, computed tomography angiography.
[a] Number of patients with measurements in both periods (before and after coronary CTA).

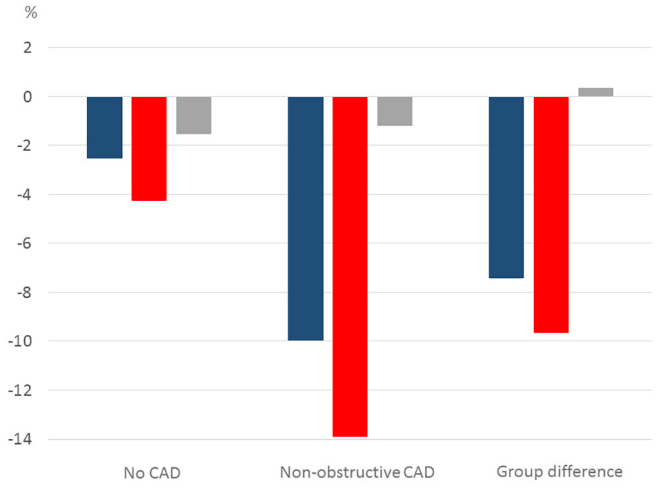

Fig. 1. Reduction in mean plasma-cholesterol and plasma-HbA1c concentrations. Numbers shown are percent reductions from 12 months before to 12 months after coronary CTA in patients with no and non-obstructive CAD as well as group differences. Reductions in plasma-cholesterol concentrations, including group differences: *P* value < 0.001. Reductions in plasma-glycated hemoglobin concentration (HbA1c) for no CAD: *P* value = 0.01. Blue = total plasma-cholesterol concentration, red = plasma-low-density lipoprotein cholesterol concentration, grey = plasma-HbA1c concentration. CTA, computed tomography angiography; CAD, coronary artery disease; HbA1c, glycated hemoglobin.

unnecessary in these low-risk patients. Future studies are warranted to explore and to better identify subgroups of patients with low risk of cardiac events assessed by coronary CTA in whom additional cardiovascular in-hospital outpatient consultations can be avoided.

5.1. Strengths and limitations

Our study has strengths and limitations. A main strength is the use of registries with high validity and comprehensiveness [11,13,14,18–20]. Moreover, all patients in Denmark have unfettered access to primary and secondary health care services [20], which reduces selection bias substantially. The study is limited by the single-center observational design as well as missing baseline data in the WDHR registry. The consequence of the latter is probably minor as the incomplete registration was random between groups [35]. Estimation of high-cardiovascular risk as defined in the present study has not been validated as a risk marker in symptomatic patients with non-obstructive CAD. The lack of full laboratory test results for all patients with chest pain is a limitation. However, the prevalence of missing data in the LABKA registry is extremely low [14]. Another potential concern is that prescription (DDDs) for preventive medical therapy is only a proxy for utilization [19]. Information on symptoms and quality of life after testing would have added valuable information to the study. Our results only pertain to the Danish and similar publically financed health care systems, where the GP is the key person in referring patients to specialized hospital treatment. We did not collect information on prognostic and economic outcomes. Further investigations are needed to determine the prognostic effect as well as the CAD preventive cost-effectiveness of coronary CTA in symptomatic patients followed-up in general practices.

6. Conclusion

In conclusion, our study shows that coronary CTA with subsequent follow-up in general practice has the potential to align health service utilization that prioritizes high-risk patients and facilitate optimized preventive management. Future studies should clarify whether these changes lead to cost-effective improvements in clinical outcomes including myocardial infarction and death.

Conflict of interest statement

The authors declare no conflict of interest.

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Appendix A

Table A1
Codes for identification of preventive medical management.

Preventive medical treatment	Drugs	ATC codes
Lipid-lowing medical therapy	Statins (HMG, CoA reductase inhibitors)	C10AA
	Fibrates	C10AB
	Nicotinic acid and derivatives	C10AD
	Other lipid modifying agents	C10AX
Anti-hypertensive medical therapy	Beta-blocking agents	C07
	Calcium channel blockers	C08
	Agents acting on the renin-angiotensin system	C09
	Diuretics	C03
	Other anti-hypertensives	C02
Anti-diabetic medical therapy	Insulins and analogues	A10A
	Blood glucose lowing agents, excl. insulins	A10B

Table A2
Coronary CTA acquisition characteristics.

	Total N = 3032	No CAD n = 2179		Non-obstructive CAD n = 853		*P* value
			Missing[a]		Missing[a]	
Heart rate, beats/min, median (IQR; range)	59 (55–65; 27–155)	60 (55–65; 27–155)	25 (1.1)	58 (54–64; 37–107)	73 (8.6)	<0.001
Sinus rhythm	2917 (96.2)	2146 (98.5)	20 (0.9)	771 (90.4)	73 (8.6)	0.125

Table A2 (*continued*)

	Total N = 3032	No CAD n = 2179		Non-obstructive CAD n = 853		*P* value
			Missing[a]		Missing[a]	
Cumulative radiation exposure, mSv, median (IQR; range)	2.3 (1.4–3.5; 0.1–29.6)	2.3 (1.4–3.5; 0.2–14.6)	366 (16.8)	2.4 (1.4–3.6; 0.1–29.6)		0.327

Values are n (%) if not stated otherwise.
CTA, computed tomography angiography; CAD, coronary artery disease; IQR, interquartile range.
[a] Missing data values in Western Denmark Heart Registry.

Table A3
Health service utilizations (number of patient consulting GP and median number of consultations) and prescriptions of medical therapy.

	No CAD n = 2179				Non-obstructive CAD n = 853			
	Before		After		Before		After	
	n (%); median	IQR; range	n (%); median	IQR; range	n (%); median	IQR; range	n (%); median	IQR; range
Health service utilizations								
Consultations with general practitioner	2122 (97.4); 5	3–9; 0–48	2008 (92.2); 4	2–8; 0–45	829 (97.2); 6	3–9; 0–51	813 (95.3); 5	3–9; 0–39
Cardiovascular admissions	441 (20.2); 0	0–0; 0–13	185 (8.5); 0	0–0; 0–8	185 (21.7); 0	0–0; 0–4	116 (13.6); 0	0–0; 0–4*
Cardiovascular outpatient consultations	1191 (54.7); 1	0–1; 0–15	450 (20.7); 0	0–0; 0–20	530 (62.1); 1	0–1; 0–14	292 (34.2); 0	0–1; 0–40***
Prescriptions medical therapy								
Lipid-lowering	624 (28.6); 0	0–26; 0–365	667 (30.6); 0	0–114; 0–365	359 (42.1); 0	0–178; 0–365	497 (58.3); 132	0–329; 0–365
Anti-hypertensive	862 (39.6); 0	0–124; 0–365	859 (39.4); 0	0–222; 0–365	477 (55.9); 25	0–333; 0–365	509 (59.7); 147	0–343; 0–365
Anti-diabetic	98 (4.5); 0	0–0; 0–365	107 (4.9); 0	0–0; 0–365	77 (9); 0	0–0; 0–365	87 (10.2); 0	0–0; 0–365

Differences in the sum of health service utilizations and prescriptions (redeemed defined daily dose) of medical therapy before as compared to after coronary CTA: if no remarks *P* value < 0.001, **P* value < 0.01, ****P* value ≥ 0.05.
CAD, coronary artery disease; CTA, computed tomography angiography.

Table A4
Health service utilizations (number of patient consulting GP and median number of consultations) (sensitivity analysis).

	No CAD n = 2179				Non-obstructive CAD n = 853			
	Before		After		Before		After	
	n (%); median	IQR; range	n (%); median	IQR; range	n (%); median	IQR; range	n (%); median	IQR; range
Health service utilizations								
Consultations with general practitioner	2122 (97.4); 5	3–9; 0–48	2016 (92.5); 5	2–8; 0–46	829 (97.2); 6	3–9; 0–51*	814 (95.4); 5	3–9; 0–40*
Cardiovascular admissions	441 (20.2); 0	0–0; 0–13	215 (9.9); 0	0–0; 0–9	185 (21.7); 0	0–0; 0–4**	129 (15.1); 0	0–0; 0–4**
Cardiovascular outpatient consultations	1191 (54.7); 1	0–1; 0–15	1793 (82.3); 1	1–1; 0–22	530 (62.1); 1	0–1; 0–14	769 (90.2); 1	1–2; 0–41

Differences in the sum of health service utilizations before coronary CTA compared to after: if no remarks the *P* value < 0.001, **P* value < 0.01, ***P* value < 0.05.
CAD, coronary artery disease; CTA, computed tomography angiography.

Table A5
Association between result of the coronary CTA and changes in health service utilizations (sensitivity analysis).

	No CAD n = 2179	Non-obstructive CAD n = 853	Odds ratios (95% CI)			
			Unadjusted	*P* value	Adjusted[a]	*P* value
Consultations with general practitioner (%)						
No change after coronary CTA	270 (12.4)	113 (13.2)	1.08 (0.85–1.37)	0.523	1.11 (0.86–1.44)	0.417
Decrease after coronary CTA	1165 (53.5)	417 (48.9)	0.83 (0.71–0.98)	0.023	0.82 (0.69–0.98)	0.028
Increase after coronary CTA	744 (34.1)	323 (37.9)	1.18 (1.00–1.39)	0.054	1.17 (0.98–1.40)	0.082
Cardiovascular admissions (%)						
No change after coronary CTA	1681 (77.1)	614 (72.0)	0.76 (0.64–0.91)	0.003	0.92 (0.76–1.13)	0.442
Decrease after coronary CTA	356 (16.3)	148 (17.4)	1.08 (0.87–1.33)	0.501	0.98 (0.77–1.24)	0.835
Increase after coronary CTA	142 (6.5)	91 (10.7)	1.71 (1.30–2.26)	<0.001	1.24 (0.91–1.67)	0.169
Cardiovascular outpatient consultations (%)						
No change after coronary CTA	705 (32.4)	265 (31.1)	0.94 (0.79–1.12)	0.494	0.95 (0.79–1.14)	0.552
Decrease after coronary CTA	420 (19.3)	136 (15.9)	0.79 (0.64–0.98)	0.033	0.78 (0.62–0.97)	0.029
Increase after coronary CTA	1054 (48.4)	452 (53.0)	1.20 (1.03–1.41)	0.022	1.22 (1.03–1.45)	0.025

CTA, computed tomography angiography; CAD, coronary artery disease; CI, confidence intervals.
[a] Logistic regression adjusted for age, male gender, high-estimated cardiovascular risk, and Charlson Co-morbidity Index score.

Appendix B

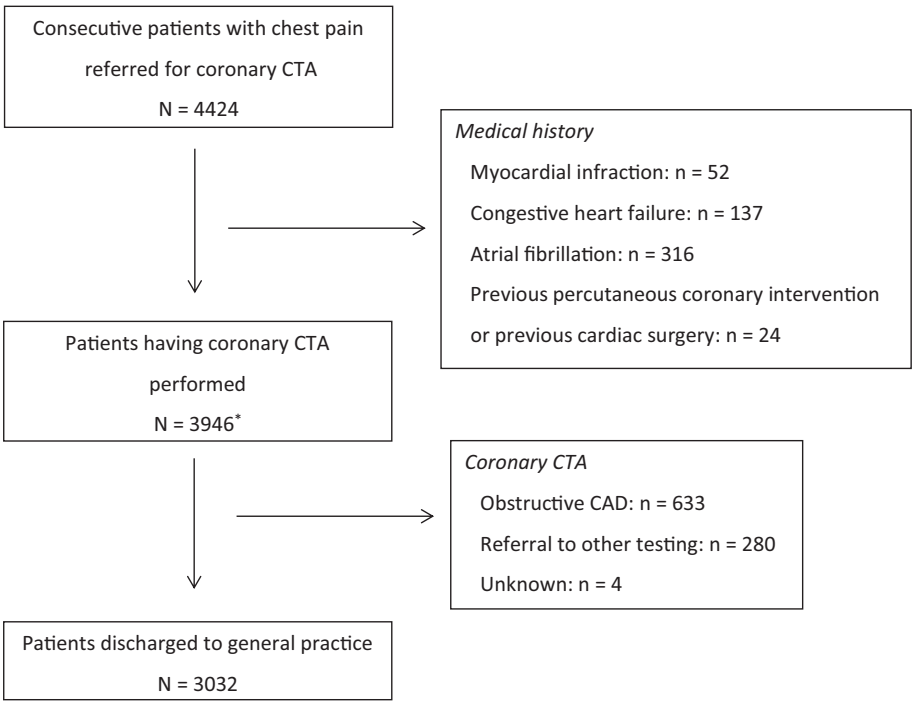

Fig. B1. Study enrollment. *The numbers do not add up because some patients have more than one of these diseases. CTA, computed tomography angiography; CAD, coronary artery disease.

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