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CLINICAL RESEARCH

High-Risk Coronary Plaque Regression After Intensive Lifestyle Intervention in Nonbstructive Coronary Disease

A Randomized Study

Jan Henzel, MD, PhD,[a,*] Cezary Kępka, MD, PhD,[a,*] Mariusz Kruk, MD, PhD,[a] Magdalena Makarewicz-Wujec, PhD,[b] Łukasz Wardziak, MD,[a] Piotr Trochimiuk, MD,[a] Zofia Dzielińska, MD, PhD,[a] Marcin Demkow, MD, PhD[a]

ABSTRACT

OBJECTIVES The authors sought to study the impact of diet and lifestyle intervention on changes in atherosclerotic plaque volume and composition.

BACKGROUND Lifestyle and diet modification are the leading strategies to manage coronary artery disease; however, their direct impact on atherosclerosis remains unknown. Coronary plaque composition is related to the risk of future cardiovascular events independent of stenosis severity and can be conveniently evaluated with computed tomography angiography (CTA).

METHODS We enrolled 92 patients (41% women; mean age 60 ± 7.7 years) with nonobstructive (<70% stenosis) coronary atherosclerosis identified by CTA. Participants were randomized (1:1) to either the DISCO (Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography) intervention group (systematic follow-up by a dietitian to adhere to the Dietary Approaches to Stop Hypertension nutrition model together with optimal medical therapy [OMT]) or the control group (OMT alone). In all patients, CTA was repeated after 66.9 ± 13.7 weeks. The outcome was change (Δ) in atheroma volume and plaque composition. Based on atherosclerotic tissue attenuation ranges in Hounsfield units (HU), the following components of coronary plaque were distinguished: dense calcium (>351 HU), fibrous plaque (151 to 350 HU), and fibrofatty plaque combined with necrotic core (-30 to 150 HU), referred to as noncalcified plaque.

RESULTS Percent atheroma volume increased in the control arm (Δ = +1.1 ± 3.4%; p = 0.033) versus no significant change in the experimental arm (Δ = +1.0% ± 4.2%; p = 0.127; intergroup p = 0.851). There was a reduction in non-calcified plaque in both the experimental arm (Δ = −51.3 ± 79.5 mm^3 [−1.7 ± 2.7%]; p < 0.001) and the control arm (Δ = −21.3 ± 57.7 [−0.7 ± 1.9%]; p = 0.018), which was greater in the DISCO intervention group (intergroup p = 0.045). No differences in fibrous component or dense calcium changes were observed between the groups.

CONCLUSIONS Controlled diet and lifestyle intervention together with OMT may slow the progression of atherosclerosis and reduce noncalcified plaque volume compared to OMT alone. (Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography [DISCO-CT]; NCT02571803) (J Am Coll Cardiol Img 2020;■:■-■)

From the [a]Department of Coronary Artery and Structural Heart Diseases, National Institute of Cardiology in Warsaw, Warsaw, Poland; and the [b]Department of Clinical Pharmacy and Pharmaceutical Care, Medical University of Warsaw, Warsaw, Poland.
*Drs. Henzel and Kępka have contributed equally to this manuscript.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CAD = coronary artery disease

CTA = computed tomography angiography

DASH = Dietary Approaches to Stop Hypertension

hs-CRP = high-sensitivity C-reactive protein

HDL = high-density lipoprotein

HU = Hounsfield units

LDL = low-density lipoprotein

OMT = optimal medical treatment

PAV = percent atheroma volume

TAV = total atheroma volume

Lifestyle and diet modification are among the leading strategies to manage coronary artery disease (CAD) (1,2). Studies have confirmed the benefit of dietary and physical activity interventions in reducing cardiovascular mortality (3–8). Postulated mechanisms include reduction of oxidative stress and amelioration of endothelial dysfunction, which may inhibit atherosclerotic plaque deposition (9–15). In addition, aggressive statin regimens and novel antiatherosclerotic therapies were shown to limit or reverse coronary atheroma progression, with resulting reduction of cardiovascular mortality (16–20). However, no data exist on the direct effect exerted by nonpharmacological intervention on coronary atheroma.

As evident from the pathogenesis of atherosclerosis, vulnerable plaques exhibit a different composition than stable lesions. Lipids and necrotic elements abundantly infiltrated by inflammatory cells are the main components of vulnerable plaques, whereas fibrotic and calcified deposits prevail in stable lesions (21,22). Recent data justify the feasibility of coronary computed tomography angiography (CTA) to evaluate plaque constitution based on differences in tissue attenuation (23–26). Furthermore, as reported by Chang et al. (24), the assessment of necrotic core and fibrofatty plaque volume may prognosticate acute coronary syndromes.

In this randomized study, we sought to evaluate the impact of diet and lifestyle modification on changes of coronary plaque components as assessed by serial coronary CTA.

METHODS

PATIENTS AND STUDY DESIGN. DISCO-CT (Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography; NCT02571803) is a pilot, single-center, randomized study of patients with suspected CAD diagnosed with CTA and qualified to conservative treatment, fulfilling specific inclusion criteria (**Table 1**). We included 92 nondiabetic patients (41% women; mean age 60 ± 7.7 years). Patients were assigned to either the experimental or control group using 10 randomization blocks of 10 participants for a 1:1 allocation ratio. All patients received optimal medical therapy. Patients allocated to the experimental arm, referred to as the DISCO intervention, were systematically followed up by a dietitian to adhere to the Dietary Approaches to Stop Hypertension (DASH) model and increase physical activity together with optimal medical therapy. Of the 91 patients who completed the observation, 2 were excluded from the analysis due to suboptimal CTA image quality. Thus, 89 patients were included in the final analysis (**Figure 1**).

In the experimental group, dietary counseling consisted of 6 sessions (**Figure 1**). In addition, patients received the dietitian's contact details (telephone number, E-mail address) to allow for extra consultations. Each patient was assigned an individual DASH nutrition plan established after body composition analysis (S10 Body Water Analyzer, InBody, Seoul, South Korea), adjusted to the basal metabolic rate and volume of physical activity. At each energy level (1600, 1800, 2000, or 2600 kcal), the following energy proportions were provided: 52% to 55% from carbohydrates, 16% to 18% from proteins, and 30% from fats. The diet was rich in fruit, vegetables, whole grains, and low-fat dairy products, and poor in saturated fats, cholesterol, low-fiber cereal products of high glycemic index, and sweets. Attention was paid to increase the number of meals up to 5 per day and to maintain the intervals between meals of <3 h. Compliance was evaluated at each visit using self-control DASH diary, 24-h nutritional interview, and the DASH index. The latter assessed adherence to the DASH plan in 8 main groups of foodstuffs (cereal products, vegetables, fruits, dairy products, meat, nuts/seeds, fats/oils, and sweets), with a maximum score of 10 per group (total 0 to 80) assigned, according to the methodology of Günther et al. (27). Interview focused on leisure time exercise was completed at each visit. Patients were asked to classify their physical activity as regular (at least 3 sessions of 30 min per week), irregular, or none. All participants were strongly encouraged to increase physical activity throughout the study, and recommendations were given in accordance with European Society of Cardiology guidelines (1,28).

Patients randomized to routine management consulted with the physician at baseline, after 6 months, and at completion of the study. Physical examination, lifestyle management, and medication checkup were performed at each visit. Dietary intervention was limited to basic counseling (i.e., no individual nutrition plan was established). Nutritional habits were assessed by the dietitian at baseline and at completion of the study using 24-h nutritional interview and the DASH index.

CTA was performed at baseline and after a mean of 66.9 ± 13.7 weeks using the 2x192-multislice scanner (Somatom Force, Siemens GmbH, Munich, Germany).

Body composition analysis and laboratory panel including lipidogram, high-sensitivity C-reactive

TABLE 1 Inclusion and Exclusion Criteria of DISCO-CT

Inclusion criteria
Coronary atherosclerosis lesions confirmed by coronary CTA defined as maximum luminal stenosis <70% in at least 2 coronary artery segments (according to ACC/AHA classification)
No indications for coronary angiography/revascularization (no documented significant ischemia of the myocardium)
Age >18 yrs
Informed consent to participate in the study
Declaration and willingness to cooperate throughout the study
Exclusion criteria
Valvular heart disease or other known condition requiring cardiac surgery (or expected cardiac surgery intervention) within 12 months
Dilated or hypertrophic cardiomyopathy
Diabetes mellitus type 2
Past CABG procedure
Known genetic disorders affecting the development of atherosclerotic lesions (e.g., familial hyperlipidemia, congenital metabolic disorders)
Factors that may affect the quality and safety of coronary CTA examination (e.g., atrial fibrillation, significant ventricular arrhythmias, poor patient cooperation, renal insufficiency, women at childbearing age) or low quality of data obtained from CTA

ACC = American College of Cardiology; AHA = American Heart Association; CABG = coronary artery bypass grafting; CTA = computed tomography angiography; DISCO-CT = Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography (NCT02571803).

protein (hs-CRP), and homocysteine were performed (Figure 1).

CTA ANALYSIS. Datasets were analyzed using a semiautomated plaque analysis software system QAngioCT version 3.1.3.13 (Medis Medical Imaging Systems, Leiden, the Netherlands). Maximum mean lumen diameter stenosis and the presence of positive remodeling were evaluated per patient using quantitative computed tomography (Syngo.via, Siemens Healthineers, Erlangen, Germany). Positive remodeling was defined as a ratio of the maximum vessel diameter at the site of lesion to the proximal reference ≥1.1. Segments of the main coronary arteries (segments 1, 2, 3, 5, 6, 7, 8, and 11) and the dominant branch of the left circumflex artery (segment 12 or 13+14/15, according to American College of Cardiology/American Heart Association classification) ≥2 mm in reference diameter were analyzed in each patient. An experienced observer blinded to allocated treatment group, patient identity, examination date, and other clinical data evaluated all of the scans.

The outcomes of analysis were changes in atheroma volume and plaque composition. Planimetry of the inner lumen and outer vessel area was performed to calculate percent atheroma volume (PAV) and total atheroma volume (TAV) (Figure 2). TAV (expressed in cubic millimeters) was calculated by subtraction of lumen volume from vessel volume. PAV was calculated by dividing TAV by vessel volume and multiplying by 100%.

In the quantitative analysis, the following components of atheroma were distinguished based on tissue attenuation ranges in Hounsfield units (HU): dense calcium (>351 HU), fibrous plaque (151 to 350 HU), fibrofatty plaque (31 to 150 HU), and necrotic core (-30 to 30 HU). The sum of fibrofatty and necrotic core volume was calculated and referred to as noncalcified plaque (-30 to 150 HU) (24). Atheroma components were expressed in cubic millimeters (raw data) and percent (normalized to vessel volume).

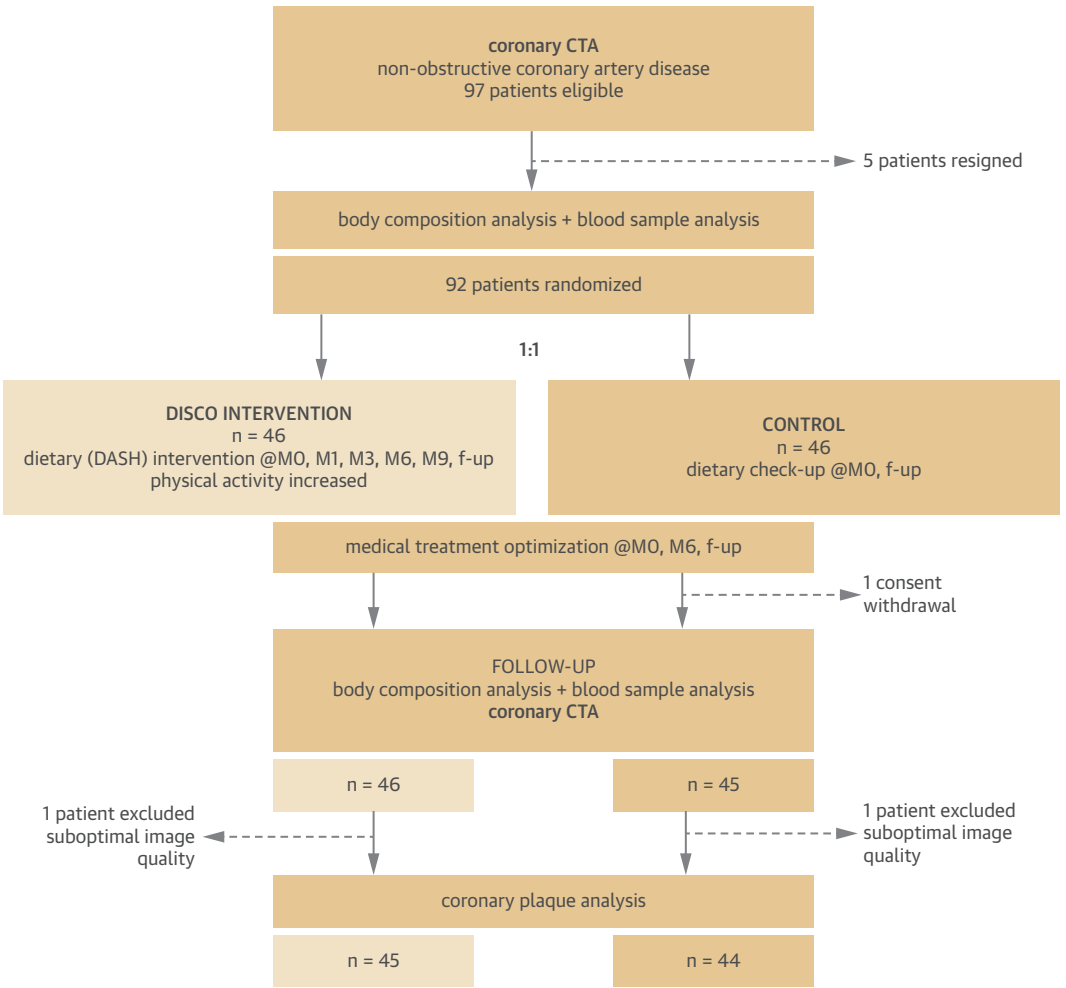
Changes in all variables were calculated as the difference in follow-up to baseline values (Δ). All analyses were performed per patient.

The analysis was repeated for 10 randomly chosen coronary CTA studies (6%) after 2 months to calculate intraobserver variability, with the observer blinded to the identities of the patients and the timing of the studies. Our results showed excellent reproducibility. Intraclass correlation coefficients (95% confidence intervals) were 0.980 (0.901 to 0.995) for the fibrous component; 0.980 (0.813 to 0.996) for the fibrofatty component; 0.925 (0.718 to 0.976) for the necrotic core; 0.985 (0.759 to 0.997) for dense calcium; 0.986 (0.947 to 0.997) for TAV; and 0.967 (0.865 to 0.992) for PAV (all $p < 0.001$).

STATISTICAL ANALYSIS. Continuous variables are presented as arithmetic mean ± SD and were compared with the Student's *t*-test when distributed normally; otherwise, median with interquartile range are presented, and the Mann-Whitney *U* test was applied. Categorical data were compared using chi-square or Fisher exact test as appropriate. The $p < 0.05$ was assumed significant. Statistical analysis was performed using SPSS software (IBM SPSS Statistics, version 21, IBM Corp., Chicago, Illinois).

TRIAL REGISTRATION AND BIOETHICS. The study was approved by the Bioethics Committee at the National Institute of Cardiology (IK-NP-0021-51/1514/15). Written informed consent was obtained from all

FIGURE 1 Flow Diagram for Study Design and Patient Allocation



CTA = computed tomography angiography; DASH = Dietary Approaches to Stop Hypertension; DISCO = Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography (NCT02571803); f-up = follow-up; M = month.

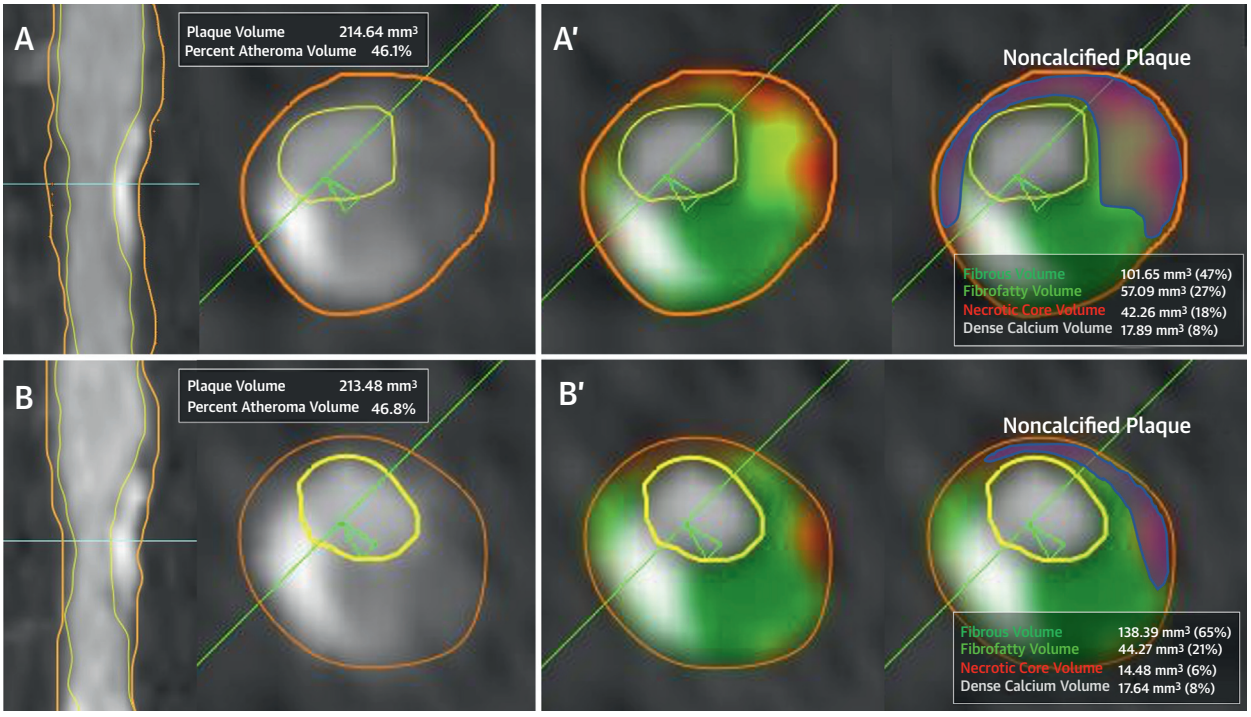
participants. The trial was registered at ClinicalTrials.gov (NCT02571803).

RESULTS

BASELINE CHARACTERISTICS. **Clinical profile.** The patients included in the study had mild anginal symptoms. No symptoms or Canadian Cardiovascular Society class 1 symptoms were reported by 93% of patients, and Canadian Cardiovascular Society class 2 symptoms were reported by 7% of patients. Four patients (4.5%) had a history of percutaneous coronary revascularization (coronary segments with previously implanted stents were excluded from analysis). Hypertension was diagnosed in 79 patients (89%) and dyslipidemia in 84 (94%). Diabetes mellitus was an exclusion criterion; however, 10 patients (11%) had prediabetes.

Medications. Fifty-six patients (64%) received an antiplatelet agent (aspirin or clopidogrel), 52 patients (58%) a beta-blocker, and 28 patients (31%) calcium-channel blocker. The median number of hypotensive drugs per patient was 2 (interquartile range 1 to 3). Sixty patients (67%) were treated with a statin, of whom 14 (16%) received high-intensity dose treatment (i.e., atorvastatin 40 to 80 mg daily or rosuvastatin 20 to 40 mg daily). Alternative lipid-lowering therapy (ezetimibe, fenofibrate) was used in 6 patients (7%), none of whom received any of the novel lipid-lowering agents.

FIGURE 2 **Demonstrative Case of Coronary Plaque Dynamics in the Middle Segment of the Left Anterior Descending Artery in a Patient Subjected to the DISCO Intervention**



Baseline **(A, A')** and follow-up images **(B, B ')** showing longitudinal **(left)** and cross-sectional views, including plaque composition analysis **(right)** using a color code with fibrotic tissue labeled in **dark green**, fibrofatty tissue in **light green**, dense calcium in **white**, and necrotic core in **red**. Noncalcified plaque (fibrofatty tissue + necrotic core) is shown in **purple**. Lumen border is marked with the **yellow line** and vessel border with the **orange line**. Despite no relevant changes in coronary plaque volume, a substantial reduction of the noncalcified plaque volume (from 45% to 27%) was revealed. DISCO = Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography.

Anthropometry. Mean body mass at baseline was 83.6 ± 15.6 kg, and mean body mass index (BMI) was 29.4 ± 4.0 kg/m^2.

No significant differences in medical history, baseline medication, and anthropometric measurements were observed between the study arms (Tables 2 and 3).

DIETARY AND LIFESTYLE INTERVENTION EVALUATION. The DASH index increased nearly 2-fold in the experimental arm (from 34.9 ± 13.8 to 59.2 ± 9.8; $p < 0.0001$) but did not change significantly in the control arm (34.1 ± 14.2 at baseline vs. 38.2 ± 12.3 at follow-up; $p = 0.138$).

The number of patients declaring any leisure time physical activity and regular physical activity increased significantly in the experimental arm ($p = 0.027$) but did not change in the control arm ($p = 0.800$) (Table 3).

TABLE 2 **Baseline Patient Characteristics**

	DISCO Intervention (n = 45)	Control (n = 44)	p Value
Female	15 (33.3)	21 (47.7)	0.121
Age at baseline, yrs	59.4 ± 8.0	60.6 ± 7.5	0.467
Previous myocardial revascularization*	3 (6.7)	1 (2.3)	0.616
Angina functional class			
No angina or CCS class 1	43 (95.6)	40 (90.9)	0.434
CCS class 2	2 (4.4)	4 (9.1)	0.434
Prediabetes	7 (11.1)	3 (6.8)	0.315
Dyslipidemia	45 (100)	41 (93.2)	0.116
Hypertension	41 (91.1)	38 (86.4)	0.522
Confirmed statin intolerance	3 (6.7)	3 (6.8)	>0.999
Atrial fibrillation	3 (6.7)	3 (6.8)	>0.999
Smoking history	27 (60)	27 (61.4)	>0.999
Observation time, weeks	69.4 ± 15.8	64.3 ± 10.7	0.078

Values are n (%) or mean ± SD. *Percutaneous coronary angioplasty only (no coronary artery bypass grafting).

CCS = Canadian Cardiovascular Society (angina grading); other abbreviation as in Table 1.

TABLE 3 Group Characteristics and Concomitant Medication at Baseline and Follow-Up

	Baseline			Follow-Up		
	DISCO Intervention (n = 45)	Control (n = 44)	p Value	DISCO Intervention (n = 45)	Control (n = 44)	p Value
Anthropometric measurements						
Total body mass, kg	84.9 ± 16.2	82.2 ± 14.9	0.415	81.3 ± 13.8	80.8 ± 14.9	0.870
BMI, kg/m^2	29.8 ± 4.2	29.1 ± 3.8	0.412	28.6 ± 3.6	28.5 ± 4.4	0.907
Systolic BP, mm Hg	129.7 ± 11.9	129.7 ± 15.5	0.999	124.8 ± 13.6	129.7 ± 14.4	0.103
Diastolic BP, mm Hg	80.4 ± 6.5	80.1 ± 8.2	0.849	76.3 ± 9.1	79.6 ± 8.1	0.075
Heart rate, beats/min	67.3 ± 7.2	65.2 ± 13.6	0.368	68.9 ± 7.6	66.6 ± 10.1	0.229
Medical treatment						
Aspirin	26 (57.8)	26 (59.1)	>0.999	31 (68.8)	31 (70.5)	>0.999
Clopidogrel	5 (11.1)	0 (0)	0.055	4 (8.9)	0 (0)	0.117
Oral anticoagulation	2 (4.4)	3 (6.8)	0.677	2 (4.4)	3 (6.8)	0.677
Beta-blocker	24 (53.3)	28 (63.6)	0.391	26 (57.8)	28 (63.6)	0.666
Calcium-channel blocker	15 (33.3)	13 (29.5)	0.808	13 (28.9)	15 (34.1)	0.628
ACE inhibitor/ARB	30 (66.6)	34 (77.3)	0.347	29 (64.4)	33 (75.0)	0.357
Diuretic	12 (26.7)	17 (38.6)	0.263	12 (26.7)	18 (40.9)	0.183
No. of antihypertensive drugs	2.0 (1.0-3.0)	2.0 (1.25 -3.0)	0.380	2.0 (1.0-3.0)	2.5 (1.0-3.0)	0.161
Metformin	5 (11.1)	2 (4.5)	0.434	5 (11.1)	2 (4.6)	0.434
Statin	29 (64.4)	31 (70.5)	0.652	36 (80.0)	34 (77.3)	0.800
High-intensity dose statin*	7 (15.6)	7 (15.9)	>0.999	10 (22.2)	8 (18.2)	0.793
Other lipid-lowering drugs†	3 (6.7)	3 (6.8)	>0.999	2 (4.4)	2 (4.5)	>0.999
Lifestyle						
Regular physical activity declared	23 (51.1)	13 (29.5)	0.052	**35 (77.8)**	**22 (50)**	**0.008**
Irregular physical activity declared	**12 (26.7)**	**23 (52.3)**	**0.017**	8 (17.8)	12 (27.3)	0.319
No leisure physical activity declared	10 (22.2)	8 (18.2)	0.793	**2 (4.4)**	**10 (22.7)**	**0.014**
Active smoking	7 (15.6)	9 (20.5)	0.591	3 (6.7)	6 (13.6)	0.315
Laboratory panel						
Total cholesterol, mg/dl	181.9 (44.4)	177.6 (42.8)	0.643	161.1 (36.9)	169.6 (35.0)	0.268
LDL,‡§ mg/dl	108.6 (37.9)	109.6 (39.6)	0.905	91.1 (30.0)	101.2 (31.1)	0.127
HDL, mg/dl	54.4 (15.0)	57.7 (14.9)	0.301	57.1 (15.8)	60.0 (16.9)	0.406
Triglycerides,§ mg/dl	72.2 (48.3)	109.1 (57.7)	0.002	96.4 (48.7)	116.2 (57.7)	0.088
hs-CRP, mg/l	0.13 (0.09-0.30)	0.14 (0.09-0.22)	0.671	0.09 (0.06-0.13)	0.12 (0.08-0.18)	**0.040**
Homocysteine, µmol/l	13.2 (4.3)	14.1 (8.7)	0.540	12.1 (3.9)	12.4 (2.5)	0.668

Values are mean ± SD, n (%), or median (interquartile range), unless otherwise indicated. The p value indicates within-group differences (paired samples Student's *t*-test or Wilcoxon paired samples test). The $p < 0.05$ marked in **bold**. *Atorvastatin 40 mg daily or more, or rosuvastatin 20 mg daily or more. †Ezetimibe 10 mg daily and/or fenofibrate 200 mg daily. ‡Calculated per Friedewald formula. §Two patients (1 from experimental arm and 1 from control arm) were excluded due to triglycerides >400 mg/dl.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; BMI = body mass index; BP = blood pressure; HDL = high-density lipoprotein; hs-CRP = high-sensitivity C-reactive protein; LDL = low density lipoprotein; other abbreviation as in Table 1.

FOLLOW-UP CHARACTERISTICS. Medical therapy was optimized throughout the study. Overall, the number of patients treated with an antiplatelet agent increased to 66 (74%), with beta-blocker increased to 54 (61%), and with a statin increased to 70 (79%), including 18 patients (20%) treated with a high-intensity dose. Differences in medication were not significant between the study arms (Table 3).

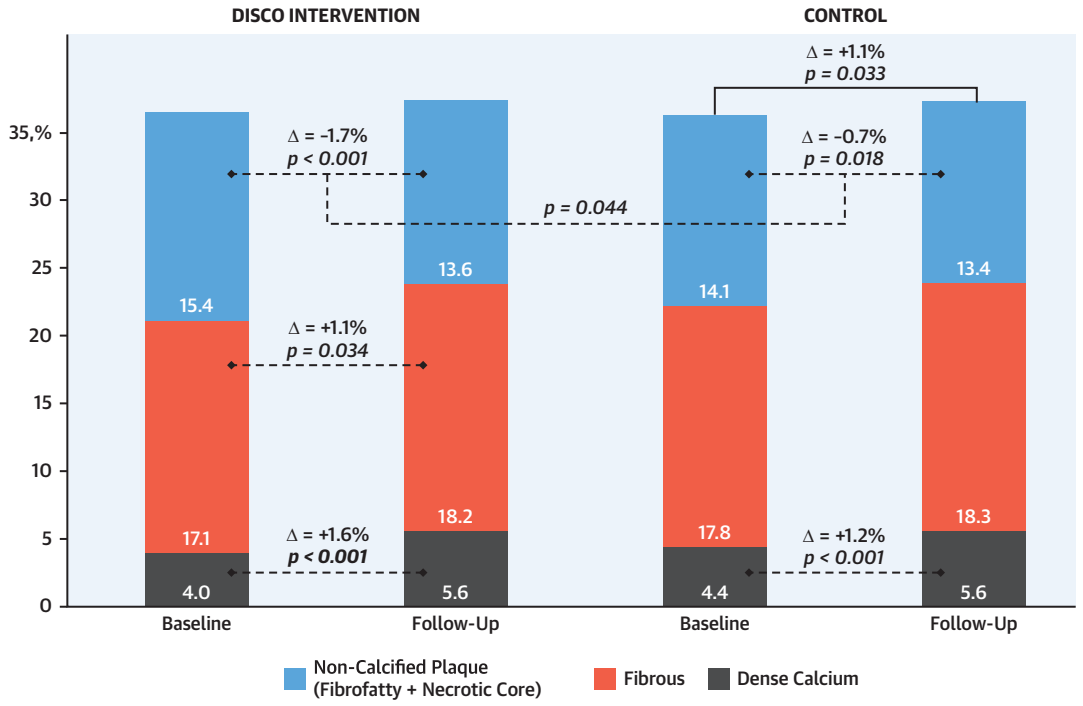
Eight patients (18%) in the experimental arm reduced BMI to <30 kg/m^2 compared to 1 patient (2%) in the control arm (intergroup p = 0.030).

Total cholesterol and low-density lipoprotein (LDL) decreased and high-density lipoprotein (HDL) increased significantly only in the experimental arm; however, intergroup analysis did not show significant differences in follow-up values (p = 0.268; p = 0.127, and p = 0.406, respectively). In turn, hs-CRP decreased significantly in the experimental arm compared to the control arm (−0.04 vs. −0.02 mg/l; p = 0.040) (Table 3).

No cardiovascular events were experienced by the participants throughout the study.

CORONARY ATHEROMA DYNAMICS. PAV increased in the control arm (Δ = +1.1 ± 3.4%; p = 0.033) versus no significant change in the experimental arm (Δ = +1.0 ± 4.2%; p = 0.127; intergroup p = 0.851). TAV did not change significantly in any arm (intergroup p = 0.458). Significant intergroup changes in plaque composition were revealed only for noncalcified

CENTRAL ILLUSTRATION **Coronary Atheroma Dynamics**



Henzel, J. et al. J Am Coll Cardiol Img. 2020;■(■):■-■.

Changes in percent atheroma volume and plaque components in the experimental (DISCO intervention) and control (CONTROL) arm. Only statistically significant changes ($p < 0.05$) are presented. DISCO = Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography.

plaque: Δ = -51.3 ± 79.5 mm^3 (−1.7% ± 2.7%) in the experimental arm versusΔ = −21.3 ± 57.7 mm^3 (−0.7 ± 1.9%) in the control arm (intergroup p = 0.045). Maximum lumen diameter decreased significantly in the experimental arm (Δ = −3.1 ± 7.2%; p = 0.007) but did not change significantly in the control arm (Δ = +2.4 ± 8.4%; p = 0.072; intergroup p = 0.025). Detailed information is presented in the **Central Illustration, Table 4**, and Supplemental Table 1.

Of note, the reduction in noncalcified plaque volume was independent of changes in body mass, BMI, total cholesterol, LDL, triglycerides, homocysteine, and calcium score (Supplemental Table 2).

DISCUSSION

DASH remains one of the most extensively studied nutritional models of proven benefit for arterial hypertension (29-32) and reduction of cardiovascular risk (4,33-35). DASH is based on common foods, is nonrestrictive, and is relatively easy to follow, with adherence comparable to or better than that of the Mediterranean diet (36). The results of our study show that a comprehensive lifestyle intervention embracing systematic dietary counseling and physical activity check (DISCO intervention) may be effective in slowing the progression of atherosclerosis and decreasing plaque vulnerability in the population of patients with nonobstructive coronary atherosclerosis.

Our findings are remarkable for several reasons: 1) this is the first study to explore the mechanistic effects and provide a pathophysiological background for the clinical benefits of diet and lifestyle intervention in coronary atherosclerosis. 2) Current findings enforce the therapeutic value of diet and lifestyle intervention together with medical management as the core ingredient of therapy. 3) The analysis highlights the role of coronary CTA as a convenient tool for noninvasive monitoring of otherwise inaccessible data on the efficacy of antiatherosclerotic therapy.

TABLE 4 Changes in Plaque Quantity and Composition in the Experimental (DISCO Intervention) and Control Arm

	DISCO Intervention (n = 45)	Control (n = 44)	p Value (Between-Groups)
PAV, %			
Baseline	36.4 ± 6.5	36.3 ± 5.9	0.896
Follow-up	37.4 ± 6.4	37.4 ± 6.4	0.988
Δ PAV	+1.0 ± 4.2	+1.1 ± 3.4	0.851
p Value (within-group)	0.127	**0.033**	
TAV, mm^3			
Baseline	972.5 ± 362.9	1,015.9 ± 276.1	0.527
Follow-up	964.6 ± 335.4	1,032.4 ± 267.8	0.294
Δ TAV	−7.9 ± 174.5	+16.5 ± 132.5	0.458
p Value (within-group)	0.763	0.412	
Plaque component volume, mm^3			
Fibrous			
Baseline	457.7 ± 187.1	497.1 ± 149.8	0.275
Follow-up	467.2 ± 161.3	504.7 ± 134.7	0.237
Δ Fibrous	+9.5 ± 117.8	+7.6 ± 92.1	0.934
p Value (within-group)	0.590	0.584	
Fibrofatty			
Baseline	374.3 ± 161.9	371.9 ± 129.7	0.939
Follow-up	331.8 ± 143.6	352.5 ± 123.5	0.470
Δ Fibrofatty	−42.5 ± 66.8	−19.4 ± 51.1	0.071
p Value (within-group)	**<0.001**	**0.015**	
Necrotic core			
Baseline	38.8 ± 43.6	33.7 ± 18.8	0.480
Follow-up	29.9 ± 21.1	31.8 ± 15.2	0.606
Δ Necrotic core	−8.8 ± 31.9	−1.9 ± 11.8	0.180
p Value (within-group)	0.072	0.297	
Dense calcium			
Baseline	101.7 ± 93.3	113.2 ± 72.1	0.516
Follow-up	135.5 ± 98.6	143.4 ± 94.0	0.700
Δ Dense calcium	+33.8 ± 68.9	+30.2 ± 52.5	0.780
p Value (within-group)	**0.002**	**<0.001**	
Noncalcified plaque volume (fibrofatty + necrotic core), mm^3			
Baseline	413.1 ± 191.6	405.6 ± 142.8	0.836
Follow-up	361.8 ± 158.2	384.3 ± 134.0	0.471
Δ Vulnerable	−51.3 ± 79.5	−21.3 ± 57.7	**0.045**
p Value (within-group)	**<0.001**	**0.018**	

Values are mean ± SD, unless otherwise indicated. The $p < 0.05$ marked in **bold**.

DISCO-CT = Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography; PAV = percent atheroma volume; TAV = total atheroma volume; other abbreviation as in Table 1.

Even though the DISCO intervention did not reduce overall coronary plaque burden, a significant increase in PAV was observed within the control arm (by 1.1%), which suggests that routine treatment may not be sufficient to stop progression of atherosclerosis. This observation is congruent with previous statin trials showing that only very aggressive medical regimens effectively reduce coronary plaque burden. As a matter of fact, plaque regression may be difficult to capture in a population with low or intermediate atherosclerosis severity as ours. Mean PAV in this study was approximately 36%, which is lower than in other trials due to a population that was not heavily burdened (17,18,37-39). Moreover, plaque regression usually is more pronounced in patients with acute presentation of CAD (40), whereas we recruited patients with clinically stable disease.

The ultimate aim of any antiatherosclerotic therapy is prevention of cardiovascular-related events, which usually is obtained by stabilization or regression of atherosclerotic plaque (22,41). Therefore, monitoring of actual coronary plaque progression may provide important pre-event information on the efficacy of therapy and guide its intensity. Plaque composition and features related to cardiovascular events are advantageously evaluable by coronary CTA and include low-attenuation component, napkin ring sign, positive remodeling, and spotty calcifications (42-45). According to our analysis, serial coronary CTA provided the critical information that therapeutic intervention led to regression of noncalcified plaque. Its reduction was very evident in the experimental group ($p < 0.001$) and was significantly greater than the reduction observed in the control group (intergroup $p = 0.045$). Importantly, this information was otherwise unobtainable and was unpredictable using more common surrogate markers, such as serum lipid changes. Therefore, our results suggest that coronary plaque composition assessment may be another potential application of coronary CTA in monitoring the efficacy of antiatherosclerotic therapies. Additional advantages of this modality include its noninvasive character and its amenability to semiautomated data analysis. Reduced radiation and contrast doses with subsequent generations of computed tomography scanners may broaden the clinical use of cardiac CTA and expand its horizons beyond the assessment of coronary stenosis.

Although coronary atheroma dynamics could be affected by concomitant medical treatment, the antiatherosclerotic medications were optimized in a sustainable way, with no relevant intergroup differences (Table 3). Overall, about 75% of patients received antiplatelet therapy and 80% received statin therapy at follow-up (20% at a high-intensity dose). Because we analyzed a population with relatively mild disease, aggressive medical treatment was not considered necessary in all cases. Additionally, a number of patients with documented statin intolerance were included (Table 2), as well as some who refused or did not adhere to the recommended pharmacotherapy. Statin treatment regimen did not affect the outcome (Supplemental Table 3). Nevertheless, this study did not analyze the effect of

medical therapy on plaque composition; rather, it compared 2 distinct lifestyle adjustment models (rigorous vs. routine), and the medical treatment was comparable between the groups.

Concurrent decrease in plaque burden and inflammatory biomarkers as the result of intensive statin therapy was reported previously (46,47). In our study, a beneficial effect on lipid profile was observed in the experimental group, with paired reductions by approximately 11% in total cholesterol, 16% in LDL, and 18% in non-HDL, approximately 2-fold greater than in the control group (**Table 3**). Even more importantly, we observed a significant reduction in hs-CRP and, as shown in our preliminary analysis, in proinflammatory cytokines (48). Whether these changes are due to the direct anti-inflammatory effect of DASH or due to the plaque healing process remains unclear; however, this trial is the first to show that nonpharmacological management results in structural changes in the coronary arteries and concomitantly reduces inflammatory response.

Analogous to previous intravascular ultrasound and CTA studies (23,26,49-52), we distinguished 4 main tissue types in the plaque constitution assessment. Based on the research by Chang et al. (24), we summed up 2 main contributors of plaque vulnerability: fibrofatty tissue and necrotic core. First, plaques abundant in these components are most likely to evolve into culprit myocardial infarction lesions and should be considered high-risk lesions. Second, plaque attenuation in CTA represents a continuum, and there may be overlap in the density strata between necrotic and low-attenuation fibrous tissue (26).

STUDY LIMITATIONS. Patients with diabetes mellitus were not included in order to make dietary management possibly uniform. Physical activity intervention was not objectified, with the investigators relying on the patients' interview declarations. Study diet intervention monitoring relied on participants' declarations, which may be misreported (53), and the nonblinded character of the study may be a source of bias. CTA-derived plaque analysis remains a surrogate endpoint, and long-term observation is necessary to ascertain the clinical benefit of the DISCO intervention in preventing cardiovascular events. Plaque attenuation thresholds are not reported uniformly across the literature, which should be taken into consideration when interpreting the results of different studies. Lastly, the sample size was small due to the pilot character of our study.

CONCLUSIONS

Intensive diet and lifestyle intervention together with optimal medical treatment may slow the progression of coronary atherosclerosis and reduce the volume of noncalcified plaque. Monitoring of coronary plaque progression by novel CTA modalities may provide unique, pre-event information on the efficacy of therapy and guide its intensity.

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AUTHOR DISCLOSURES

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ADDRESS FOR CORRESPONDENCE: Dr. Cezary Kępka, Department of Coronary Artery and Structural Heart Diseases, National Institute of Cardiology in Warsaw, 42 Alpejska St, 04-628 Warsaw, Poland. E-mail: ckepka@ikard.pl.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: A comprehensive, individualized lifestyle intervention may lead to beneficial changes in coronary plaque volume and composition, as assessed by CTA.

TRANSLATIONAL OUTLOOK: Plaque constitution analysis may be a useful modality in identification of high-risk lesions. Further research is necessary to ascertain the prognostic value of plaque constitution analysis by CTA.

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KEY WORDS coronary artery disease, coronary computed tomography, DASH diet, lifestyle Intervention, vulnerable plaque

APPENDIX For supplemental tables, please see the online version of this paper.