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Association Between Changes in Coronary Artery Disease Progression and Treatment With Biologic Agents for Severe Psoriasis

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IMPORTANCE Inflammatory pathways of psoriasis share similarities with the mechanisms identified in atherosclerosis, and the association between psoriasis and cardiovascular disease due to accelerated coronary artery disease is well established. The effect of anti-inflammatory drugs on the development of coronary atherosclerosis remains essentially unknown.

OBJECTIVE To investigate the association of biological therapy with changes in coronary artery disease progression, measured by repeated coronary computed tomography (CT).

DESIGN, SETTING, AND PARTICIPANTS This single-center prospective, controlled, observer-blinded clinical study at a tertiary dermatology university hospital clinic enrolled patients with severe psoriasis initiating biological therapy and matched controls not receiving systemic therapy from April 11, 2011, through June 30, 2014.

INTERVENTIONS Biological therapy approved for psoriasis (adalimumab, etanercept, infliximab, ustekinumab) with the possibility to switch between treatments to ensure tight control of inflammation.

MAIN OUTCOMES AND MEASURES Patients underwent noncontrast coronary artery calcium (CAC) CT and contrast-enhanced coronary CT angiography at baseline and after 13 months of follow-up. Changes in CAC score, number of coronary plaques, severity of narrowing, composition, and vessel wall volume were measured.

RESULTS There were 28 treated patients (mean [SD] age, 49.2 [10.2] years; 71% men; mean [SD] Psoriasis Area Severity Index [PASI], 15.4 [4.3]) and 28 controls (mean [SD] age, 52.8 [10.6] years; 71% men; mean [SD] PASI, 12.4 [3.9]). The CAC scores remained stable in the intervention group (mean [SD] yearly CAC change, −16 [56]; $P = .15$) and progressed in the control group (14 [29]; $P = .02$) (intervention vs controls: $P = .02$). The number of segments with luminal abnormalities remained unchanged in both groups. The severity of luminal narrowing in the diseased segments was unchanged in the intervention group (Wilcoxon W = 76, n = 483, $P = .39$) but increased at follow-up in the control group (Wilcoxon W = 281, n = 414, $P = .02$). Automated vessel wall volume index remained unchanged from baseline to follow-up in the intervention group (mean [SD] baseline, 7.1 [1.5], follow-up, 7.1 [1.7]; $P = .91$), while controls demonstrated statistically nonsignificant progression (baseline, 8.3 [1.6], follow-up, 8.9 [2.2]; $P = .06$).

CONCLUSIONS AND RELEVANCE Clinically effective treatment with biologic agents was associated with reduced coronary artery disease progression in patients with severe psoriasis. These findings support a beneficial effect of biologic anti-inflammatory agents in preventing cardiovascular disease progression in addition to disease control in inflammatory diseases.

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Biological agents with effect on inflammatory processes, for example, tumor necrosis factor (TNF) inhibitors, are effective for treating diseases involving autoimmune reactions such as psoriasis,[1-3] rheumatoid arthritis,[4] and inflammatory bowel disease.[5] Several of these diseases are associated with premature occurrence of coronary artery disease (CAD),[6-9] which is suspected to be associated with the underlying inflammatory pathophysiologic mechanisms of these diseases.[10] The concept of atherosclerosis as an inflammatory disease is based on observations of immune activation in human atherosclerotic lesions, on recognition of inflammatory biomarkers as independent risk factors for cardiovascular events, and on evidence of immune activation induced by low-density lipoproteins.[11,12] Evidence supporting the use of anti-inflammatory therapy for atherosclerosis rests mainly on observational and small interventional studies evaluating surrogate markers of disease activity, but it is unknown whether these findings may translate into modulation of the progression of CAD.[13,14]

The inflammatory pathways of psoriasis share similarities with the mechanisms identified in atherosclerosis.[15] There is evidence of systemic inflammation in psoriasis,[16] and the association between psoriasis and cardiovascular disease due to accelerated CAD is well established.[17] However, it remains unknown whether modification of the inflammatory activity modifies the progression of the accelerated atherosclerotic process.

The aim of our study was to investigate whether biologic antipsoriatic treatment may affect the progression of coronary atherosclerosis in patients with moderate to severe psoriasis assessed from repeated coronary computed tomography (CT).

Key Points

Question Does modulation of inflammation by treatment with biologic agents affect the progression of coronary artery disease in patients with severe psoriasis?

Findings In this clinical study, at the end of 13 months' follow-up, reduced coronary artery disease progression was observed in patients with severe psoriasis who were treated with biologic agents compared with controls. Repeated coronary computed tomographic angiography showed significant reduced progression of coronary plaque severity, and reduced progression of calcium scores.

Meaning In addition to disease control, treatment with anti-inflammatory biologic agents may reduce coronary artery disease progression in patients with severe psoriasis.

Methods

Study Design and Protocol

This study was a prospective, controlled, observer-blinded, interventional clinical study in patients with severe psoriasis initiating treatment with biological therapy as the intervention group. Patients with equally severe psoriasis not receiving systemic therapy or phototherapy formed the control group.

All patients were examined with coronary CT at baseline and after approximately 1 year of follow-up. The intervention group comprised patients initiating treatment with biological agents approved for psoriasis, that is, adalimumab, etanercept, infliximab, and ustekinumab. The choice of drug was not mandated by the study protocol but decided on an individual basis following national guidelines. In case of insufficient efficacy, defined as a Psoriasis Area Severity Index (PASI) reduction of less than 50%, or adverse effects of the biological agent, the patients could be switched to one of the other drugs at the treating physician's discretion. Such transition was also conducted according to national guidelines. The controls were patients with similar disease activity who were found eligible for systemic antipsoriatic therapy but declined systemic treatment for personal reasons and therefore received no treatment or topical therapy only.

The Central Denmark Region Committees on Biomedical Research Ethics and the Danish Data Protection Agency approved the study protocol before enrollment commenced. All participants provided written informed consent before entering the study. The trial was registered at http://clinicaltrials.gov, identifier NCT01356758.

Patients

The inclusion and exclusion criteria have been described previously.[6] Patients older than 18 years with moderate-to-severe psoriasis vulgaris with PASI of at least 10 were eligible if they had no symptoms of CAD, no major uncontrolled cardiovascular risk factors, and no prior cardiovascular events or coronary artery revascularization. Additional eligibility criteria and details on clinical assessments are provided in the eMethods in the Supplement.

CT Procedures

Patients underwent noncontrast coronary artery calcium (CAC) CT and contrast-enhanced coronary CT angiography (CCTA) at baseline and after approximately 1 year of follow-up. Electrocardiogram-gated CCTA was conducted during a single breath-hold using a dual-source CT system (SOMATOM Definition; Siemens). Electrocardiogram-dependent tube current modulation (Care Dose 4D) was used as default in all patients (reference, 320 mAs). Tube voltage was set at 100 or 120 kV (peak). Detector collimation was 2 × 64 × 0.6 mm; gantry rotation time was 330 milliseconds. Patients were given 1 or 2 doses (0.4-0.8 mg) of nitroglycerin spray solution sublingually before the procedure. Pharmacological heart rate control was used when appropriate. The contrast medium comprised 70 to 80 mL of Optiray (Ioversol 350 mg iodine/mL, Mallinckrodt Medical Gmbh). Data sets were reconstructed with a slice thickness of 0.75 mm (reconstruction increment, 0.4 mm) using dedicated cardiac filters (B35f and I26f).

Coronary Artery Calcium Score

CT images were analyzed using the imaging software syngo.via (Siemens Healthcare, Siemens AG). Using the noncontrast data, identification was performed on each calcified lesion in each vessel (right coronary artery, circumflex, left main coronary

artery, and left anterior descending artery). A CAC score was obtained by a semiautomated algorithm in accordance with the Agatston method.[18] Settings were as follows: threshold, 130 HU 96.5 mg/cm^3 calcium hydroxylapatite and mass calibration factor, 0.743.

Coronary Artery Angiography Analysis

Transaxial, horizontal, and sagittal contrast images were evaluated together with reconstructed images using multiplanar reformation.

The coronary tree was divided into an 18-segment model[19] based on the axial coronary segmentation model suggested by the American Heart Association[20] (see eFigure in the Supplement). An expert observer (M.B.) blinded to the identity and allocation of the patients performed all analyses. Segments 2.0 mm or greater in diameter were analyzed and categorized according to the following attributes: (1) segment analyzability, (2) presence of plaques, (3) luminal stenosis and quantitative area stenosis graded according to an ordinal scale (no plaque; 0% stenosis; mild [1%-49%] stenosis; moderate [50%-69%] stenosis; severe [70%-100%] stenosis), and (4) plaque composition (calcified, mixed, noncalcified). Plaques were visually identified on the contrast-enhanced CT. Noncalcified plaques were identified as structures adjacent to or compromising the coronary artery lumen with lower density than the contrast-enhanced vessel lumen and clearly distinguished from the surrounding tissue. Calcified plaques were identified similarly, but with a higher density than the contrast-enhanced vessel lumen.

Vessel Wall Volume Index Analysis

Analysis was performed with a Vitrea fX workstation and the SUREplaque software (Vital Images), which are not approved for clinical use but have been validated in several studies.[21,22] The method of analysis was adopted from Kwan et al[23] (eFigure in the Supplement).

All vessels were analyzed from the beginning of the ostium to a distal luminal diameter of 2.0 mm or until artifacts corrupted the measurements. In multiphase CT investigations, all available phases were reviewed to determine the optimal phase for vessel contouring. All automated contouring of the external vessel wall and internal lumen was manually reviewed. Only vessels and segments appropriately contoured by the automated software were included in the analysis. The vessel was excluded if the automated software failed to determine the true location of its boundaries. If a vessel was excluded either at baseline or follow-up CT, the corresponding vessel would be excluded from the paired investigation. Vessel wall volume was calculated by subtracting the lumen volume from the total vessel volume. Vessel wall volumes were normalized by coronary artery length to determine the vessel wall volume index (VWVI) (in square millimeters). Plaque subtypes have previously been defined[22] as "soft" plaque (–100 to 30 HU), "fibrous" plaque (>30 but <150 HU), and "calcified" plaque (150-1300 HU).

Statistics

We calculated that a sample size of 27 patients in each group would provide a power of 80% to detect a clinically relevant difference in the CAC score increase between groups. The intended sample size was 30 patients in each group to allow for a 10% dropout rate. Assuming a mean (SD) baseline calcium score of 100 (40) and an increase to 110 (40) after 1 year in the intervention group, the control group would need to increase to a mean (SD) of 135 (40) to detect a statistically significant difference at a 2-sided α level of .05.

Patient characteristics were compared using the *t* test for continuous variables and χ^2 statistics for categorical variables. Within-group differences between baseline and follow-up CAC scores were computed using the *t* test for paired samples. Between-group comparison of changes in CAC scores was computed using an unpaired *t* test with the Welch correction due to unequal variances. Differences in number of segments with luminal narrowing and severity of abnormalities between baseline and follow-up were expressed as ordinal data and calculated using the Wilcoxon matched-pairs signed rank test. The VWVI data and laboratory values were compared using paired-sample *t* tests and unpaired *t* tests with equal variances. The level of statistical significance was set at α = .05. Graphs and statistical analyses were made in GraphPad Prism, version 6.0 (GraphPad software), and STATA/IC, version 12.1 for Mac (StataCorp).

Results

Study Participants

From April 11, 2011, through June 30, 2014, we assessed 84 patients for eligibility. Of 58 patients enrolled, 30 initiated biologic treatment and 28 were observed as controls (Consolidated Standards of Reporting Trials [CONSORT] flow diagram, eFigure in the Supplement). Baseline characteristics of study participants were similar in the 2 groups (**Table 1**). The mean (SD) follow-up was 13.4 (1.7) months. Two patients in the intervention group and none in the control group discontinued participation prematurely as a result of personal/family reasons or logistics.

Treatment During Study

All intervention group patients initiated treatment the day of their baseline coronary CT or within less than 2 weeks of that day. Adalimumab treatment was initiated in 21 patients. Among these, 17 continued taking this drug, while 2 switched to etanercept, 1 to ustekinumab, and 1 to infliximab. One patient started by taking infliximab and switched to adalimumab during the study. Three patients started by taking etanercept and another 3 ustekinumab without any switch during follow-up. Disease control in the intervention group was good during the study period (**Figure 1**), with a mean (SD) PASI reduction of 87.6% (14.8), and 82% of patients achieved at least a 75% PASI reduction. None of the control patients initiated systemic antipsoriatic treatment, other immunosuppressive therapy, or photo/photochemotherapy during the study.

Effect of Biologic Agents on Cardiac Computed Tomography Findings

The results of CAC CT are shown in **Figure 2**. Mean (SD) baseline CAC scores did not differ between the groups (intervention group, 98 [282]; controls, 77 [178]; *P* = .75). The CAC scores remained stable in the intervention group at follow-up (mean [SD] yearly CAC change, –16 [56]; *P* = .15) and progressed in the control group

Table 1. Patient Characteristics and Traditional Cardiovascular Risk Factors[a]

Variable	Intervention Group (n = 28)	Control Group (n = 28)
Age, mean (SD), y	49.2 (10.2)	52.8 (10.6)
Male sex, No. (%)	20 (71)	20 (71)
Psoriasis Area Severity Index, mean (SD)	15.4 (4.3)	12.4 (3.9)
Disease duration, mean (SD), y	25.2 (13.4)	31.7 (15.0)
Blood pressure, mean (SD), mm Hg		
Systolic	137.6 (14.2)	139.3 (13.4)
Diastolic	85.2 (10.7)	86.9 (8.4)
BMI, mean (SD)	29.3 (5.9)	28.8 (6.2)
Family history of ischemic heart disease, No. (%)	11 (39)	14 (50)
Tobacco use, No. (%)		
Ever smoked[b]	13 (46)	20 (71)
Current smoker	7 (25)	7 (25)
Medically treated conditions, No. (%)		
Diabetes	2 (7)	2 (7)
Hyperlipidemia	5 (18)	4 (14)
Hypertension	7 (25)	7 (25)
Cholesterol level, mean (SD), mg/dL		
Total	208.5 (27.8)	220.1 (44.0)
Low-density lipoprotein	127.4 (25.9)	135.1 (35.1)
High-density lipoprotein	50.2 (17.0)	57.9 (16.2)
Follow-up time, mean (SD), d	397.0 (46.4)	401.4 (57.8)

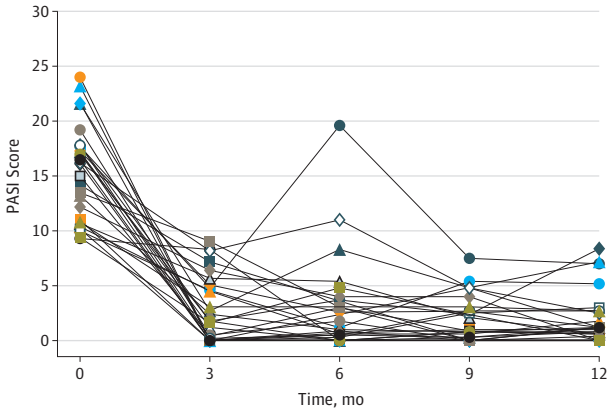
Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

SI conversion factor: To convert cholesterol to millimoles per liter, multiply by 0.0259.

[a] There were no significant differences between the groups at baseline except for PASI (P = .01).

[b] Defined as current tobacco use or smoked at least 100 cigarettes/ approximately 100 g of tobacco during course of life.

Figure 1. Psoriasis Area Severity Index (PASI) During Treatment With Biological Agents



Disease control was generally tight, with switch in biologic treatment when less than a 50% reduction in PASI was obtained or in case of adverse events. Symbols represent individual patients, and lines connect paired observations for each patient.

(mean [SD] yearly CAC change, 14 [29]; P = .02). Between-group comparison of differences from baseline to follow-up showed a significantly increased progression of CAC among controls compared with the intervention group (mean CAC difference between groups, 29.9 [95% CI, 5.6-54.1]; P = .02).

The CCTA data are shown in **Figure 3**. The number of segments with luminal narrowing did not change from baseline to follow-up in either group (Figure 3A). Overall, we found 6.4% of segments with luminal narrowing among all analyzable segments at baseline in the intervention group; this remained unchanged at 6.2% at follow-up (P = .38). Among controls, 7.7% of segments had luminal narrowing at baseline. This increased, albeit insignificantly, to 9.6% at follow-up (P = .14).

The progression of narrowing seemed to be attenuated among patients treated with biologic agents as no significant difference in the severity of narrowing from baseline to follow-up was observed (Wilcoxon W = 76, n = 483, P = .39). In contrast, progression of narrowing was significantly increased in the control group at follow-up (Wilcoxon W = 281, n = 414, P = .02) (Figure 3B).

Overall, the analysis of VWVI data showed a similar pattern (**Table 2**). In the intervention group, the mean (SD) total VWVI remained unchanged from baseline to follow-up (7.1 [1.5], follow-up 7.1 [1.7]; P = .91), and subanalysis at vessel and composition level indicates that the progression was halted in the intervention group. Among controls, mean (SD) total VWVI progressed, but the increase was not statistically significant (mean [SD] baseline, 8.3 [1.6], follow-up 8.9 [2.2]; P = .06). Subanalysis showed a significant increase in VWVI for the right coronary artery among controls (P = .04) and a significant increase in the soft component of the vessel wall (P = .002). Between-group comparison indicated a significant increment of the progression of the soft wall component in controls compared with the intervention group (mean difference, 0.4 [95% CI, 0.1-0.7]; P = .02).

Image quality and analyzability were similar in the 2 groups (eAnalyzabilty in the Supplement).

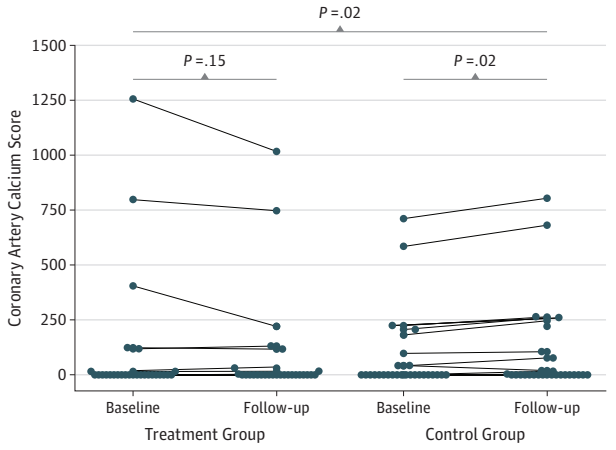
Changes in Acute-Phase Proteins and Lipids

In the intervention group, the mean (SD) serum levels of C-reactive protein decreased from baseline to follow-up (3.9 [3.9] vs 2.4 [3.4] mg/L; P = .04 [to convert to nanomoles per liter, multiply by 9.524]), and they remained unchanged among controls (2.5 [2.5] vs 2.9 [2.7] mg/L; P = .13). Between-group analysis showed a significant decrease in C-reactive protein level in the intervention group compared with controls (mean difference, 1.9 [95% CI, 0.4-3.4] mg/L; P = .01). Compared with baseline levels (Table 1), mean (SD) lipid levels remained unchanged in both groups at follow-up (intervention group: total cholesterol, 212.4 [30.9] mg/dL, P = .61, low-density lipoprotein cholesterol, 131.3 [27.0] mg/dL, P = .83, high-density lipoprotein cholesterol, 54.1 [15.4] mg/dL, P = .49; controls: total cholesterol, 204.6 [38.6] mg/dL, P = .19, low-density lipoprotein, 127.4 [34.8] mg/dL, P = .13, high-density lipoprotein, 54.1 [15.4] mg/dL, P = .22 [to convert to millimoles per liter, multiply by 0.0259]).

Secondary Analysis of CCTA Outcomes

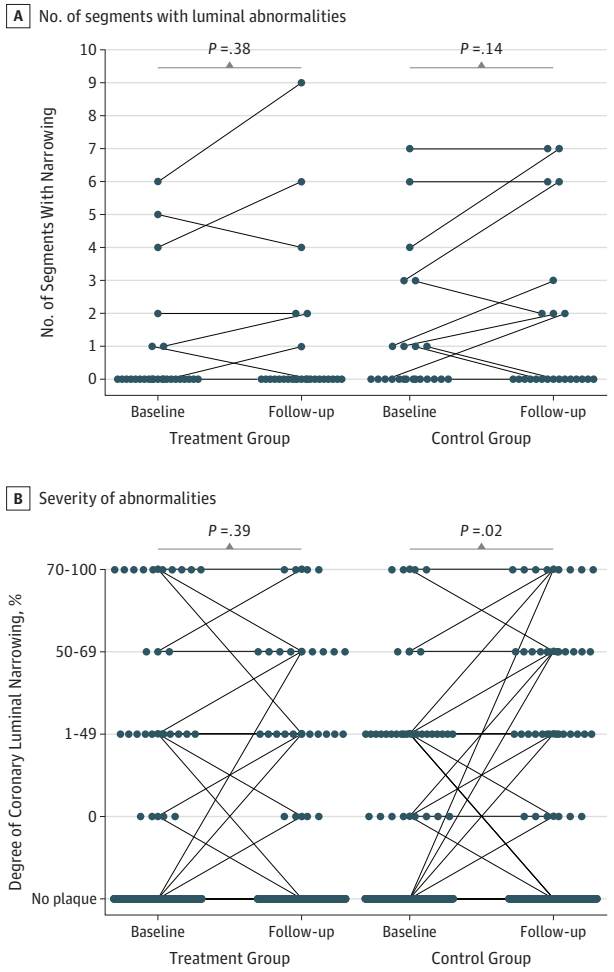
Additional analysis after exclusion of patients receiving ustekinumab during follow-up and patients achieving less than a 75% PASI response is presented in the eResults in the Supplement.

Figure 2. Coronary Artery Calcium Scores at Baseline and Follow-up



The progression of coronary calcium scores from baseline to follow-up in both groups is shown. Results of repeated-measures statistics and between-group statistics are shown. Symbols represent individual patients, and lines connect paired observations for each patient.

Figure 3. Number of Segments With Luminal Abnormalities and Severity of Abnormalities at Baseline and Follow-up



A, Number of segments with luminal narrowing on a patient level at baseline and at follow-up. Lines symbolize a change in the number of segments with abnormalities for 1 or more patients. B, Severity of the luminal narrowing for all analyzable segments on an ordinal scale. Symbols represent individual segments, and lines represent the change in severity of luminal narrowing for 1 or more segments.

Discussion

In this study of patients with moderate-to-severe psoriasis, clinically effective antipsoriatic treatment with biological agents was associated with reduced coronary atherosclerosis progression in patients without symptomatic CAD during a mean 13-month follow-up period. Patients with psoriasis have an increased prevalence of premature CAD compared with a matched background population.[6] We studied patients with psoriasis who were at increased risk of premature CAD before and after 1 year of new-onset treatment with biological agents and evaluated asymptomatic coronary atherosclerosis progression. Because the progression rate remains undefined in this patient group, we compared it with the natural progression in a comparable control group of patients continuing topical therapy only. While atherosclerosis progressed slowly in the control group, progression of CAC was attenuated in patients initiating biological treatment. Similarly, the progression of other coronary atherosclerosis variables including the severity of luminal abnormalities and the vessel wall volume progressed in control patients but not in patients initiating biological treatment. Our findings indicate that biological agents may attenuate coronary atherosclerotic disease progression.

Secondary analysis showed that exclusion of patients achieving a PASI response of between 50% and 75% did not affect the main outcomes. Excluding patients treated with ustekinumab, leaving only anti-TNF–treated patients in the analysis, showed a slightly increased difference in vessel wall volume outcomes compared with controls.

The results of the present study are strengthened by the simultaneous use of 3 different, independent cardiac CT modalities that consistently demonstrated decreased CAD progression among patients treated with biologics. The findings were corroborated by a reduction in acute-phase proteins in intervention patients compared with controls.

Previous observational data suggest that treatment with anti-TNF agents[24-27] and methotrexate[28,29] may have a protective effect on cardiovascular disease in patients with inflammatory diseases. Thus, these and other observational studies show a beneficial effect of both drugs on cardiovascular outcomes, that is, fewer cardiovascular events. The findings are supported by studies in soluble inflammatory biomarkers,[30-32] insulin sensitivity,[33] carotid intima media thickness,[34-36] and myocardial dysfunction[37] showing a beneficial effect of anti-TNF agent use. However, because of the inherent limitations of observational studies and absence of solid clinical data and randomized clinical trials, firm conclusions cannot be drawn.[14]

We used psoriasis as a model of a well-defined inflammatory disease with a systemic component and an acknowledged

Table 2. Vessel Wall Volume Index Results at Baseline and Follow-up

Measurement	Treated With Biologic Agents			Controls			*P* Value for Treated vs Controls
	Mean (SD)			Mean (SD)			
	Baseline	Follow-up	*P* Value	Baseline	Follow-up	*P* Value	
Vessel wall volume index, mm^2							
Total	7.1 (1.5)	7.1 (1.7)	.91	8.3 (1.6)	8.9 (2.2)	.06	.08
Vessel							
Left anterior descending artery	6.3 (1.5)	6.5 (1.4)	.35	8.0 (2.0)	8.3 (2.1)	.33	.94
Circumflex	8.7 (2.5)	8.6 (2.7)	.76	8.7 (1.1)	9.1 (1.7)	.24	.30
Right coronary artery	6.6 (2.2)	6.6 (2.3)	.91	8.1 (2.5)	9.1 (3.2)	.04	.11
Composition, mm^2[a]							
Soft	2.5 (0.6)	2.5 (0.6)	.73	2.6 (0.6)	2.9 (0.6)	.002	.02
Fibrous	3.7 (1.0)	3.7 (0.9)	.86	4.5 (0.9)	4.8 (1.3)	.08	.44
Calcified	0.9 (1.0)	1.0 (0.9)	.65	1.2 (0.7)	1.1 (0.9)	.76	.38

[a] Values correspond to the normalized volume of the vessel: volume in cubic millimeters normalized by length in millimeters.

association with increased cardiovascular risk.[16,17] The advantages of psoriasis as a model are the easy access to monitor disease activity[38] and the availability of high-efficacy treatments. The study was designed to evaluate the effect of biological agents on CAD progression without interference due to introduction of other secondary preventive measures during follow-up, for example, initiation of statin treatment. For ethical reasons, we included asymptomatic patients only. Furthermore, patients with prior cardiovascular events or prior coronary intervention were excluded due to the potentially limited diagnostic usefulness of CCTA in such patients. Because this restriction reduced the number of patients with known CAD, it remains unknown whether inclusion of such patients might have translated into a stronger signal with respect to the beneficial effect of biological treatment. Hence, our study should therefore be considered exploratory and hypothesis generating to justify a randomized study testing the efficacy of biological treatment for attenuating CAD progression in patients with psoriasis stratified by symptomatic or nonsymptomatic CAD.

Coronary CT is a well-established noninvasive method for risk assessment and a diagnostic tool in suspected CAD. Coronary artery calcium scoring predicts future ischemic heart disease and cardiac outcome across all age and ethnic groups.[39-41] Repeated CAC measurement is characterized by low interscan and interobserver variability.[42] Contrast-enhanced coronary CT enables noninvasive vessel wall visualization and allows for distinction between different plaque types.[43,44] Furthermore, CCTA adds prognostic information as nonobstructive and obstructive CAD by CCTA are associated with increased mortality rates.[45] A combination of CAC scoring and CCTA, as used in the present study, has additive value for predicting major cardiovascular events.[46] An advantage of the software used for detection of the vessel wall volume is the automatic vessel contouring with no manual editing of boundaries, which makes the results reproducible with low intraobserver and interobserver variability.[21]

Patient adherence to protocol was adequate. The use of a paired approach minimized random interindividual variation. The between-group comparison allowed for evaluation of the difference in progression rather than for comparison of the level of CAD, which minimizes the effect of random variation.

An obvious limitation of the present study is the limited number of patients. The observational nature of the study and the exposure to radiation restricted the number of patients that could be enrolled due to ethical considerations. Although our study was not randomized, matching of our patient groups was successful with respect to all known cardiovascular risk factors. However, in combination with the open-label design, a risk of bias is present, in particular, observer bias and selection bias. Yet, the group allocation of patients was blinded to the physician during CT data analysis, and baseline and follow-up investigations were evaluated at distinct time points, making biased assessments less likely. The differences in disease progression could, in part, be argued to reflect differences in atherogenic risk profile between groups rather than effect of biologic treatment. However, there were no significant differences between groups in the baseline levels of lipids, blood pressure, or blood glucose and no differences in the number of patients classified as having medically treated hyperlipidemia or hypertension or current smokers. In controls, a slight nonsignificant reduction in total cholesterol and low-density lipoprotein cholesterol levels was observed at follow-up, making it unlikely that the relatively increased CAD progression in this group is caused by a more atherogenic risk profile.

The generalizability of the results may be limited to patients with moderate-to-severe psoriasis without known CAD. It is unknown whether a similar response may be extended to patients with other inflammatory diseases. Finally, it remains unknown to what extent the finding of reduced CAD progression translates into a reduced risk of cardiovascular events.

Conclusions

Our data provide pathophysiological evidence that anti-inflammatory biologic treatment may prevent asymptomatic coronary atherosclerosis progression in patients with moderate-to-severe psoriasis.

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NOTABLE NOTES

The Keloid Scars of Slavery

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Sethe, the protagonist of Toni Morrison's *Beloved,* suffers from a dermatologic entity common to many African Americans: a keloid. While a slave on a plantation, she was assaulted by 2 white men. When Sethe informs her mistress of the attack, her master punishes her further, ordering Sethe to be whipped. This brutality scars her back and ultimately develops into a keloid in the shape of a "chokecherry tree."[1] Throughout the novel, Sethe's "tree" serves as a direct representation of the cruelty of slavery and becomes a constant reminder of its impact on Sethe's psyche.

Morrison was not the first to represent the cruelty of slavery through keloid scarring. In 1863, *Harper's Weekly*, an American political magazine popular during the Civil War, demonstrated slavery's brutality with photographs of "Whipped Peter," an escaped Louisiana slave named Gordon who was ruthlessly beaten. The photographs of his severe keloids were later used throughout the United States by abolitionists, such as William Lloyd Garrison and Henry Ward Beecher, to provide visual evidence of the inhumanity of slavery. They claimed it was "symbolic of the brutality of the slave system, and of the society that sustains it."[2]

In both Morrison's *Beloved* and the historical account of "Whipped Peter," keloids are more than scars; they symbolize the complex history of slavery. For Sethe, they are a constant reminder of the physical and psychological cruelty of slavery, while for Gordon, his keloids became a call for abolition.

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