SUPPLEMENTAL MATERIAL

Baggish AL, Weiner RB, Kanayama G, Hudson JI, Lu MT, Hoffmann U, Pope HG, Jr. Cardiovascular toxicity of illicit anabolic-androgenic steroid use

This supplementary material has been provided by the authors to provide readers with additional information about their work.

CONTENTS

Appendix A – Supplementary Methods

Transthoracic Echocardiography (TTE).

Image Acquisition. Cardiac ultrasound imaging was performed with a commercially available echocardiography system (iE-33, Phillips Medical Systems, Netherlands) with a 1.9- to 3.8-mHz phased-array transducer. Participants were imaged at rest ≥ 12 hours after their most recent exercise or weightlifting sessions. Two-dimensional imaging was performed from standard parasternal and apical transducer positions with frame rates confined to 60-100 Hz as determined on an individual subject basis for image optimization. All data were stored digitally and image analysis was performed using commercially available software on a dedicated work-station (Xcelera, Version 3.2.1.7-12-2011, Phillips Medical Systems, Netherlands). Images were analyzed with investigators blinded to subject AAS use status.

Image Analysis. Cardiac structural and functional measurements were made in accordance with current guidelines.[1, 2] Left ventricular (LV) volumes and ejection fraction were measured and calculated with the modified Simpson biplane technique. For the primary outcome variable LV ejection fraction, a value of ≥52% was used to define the lower limits of normal (Figure 1, main text).[1] LV mass was calculated using the area-length method, which was chosen because it accounts for LV morphology in both short- and long-axis dimension. Myocardial tissue velocities were measured using pulse wave Doppler tissue imaging with sampling at the acquired from apical 4-chamber view with frame rates ≥ 120 Hz. Reported tissue velocities represent the average of 3 consecutive cardiac cycles. The primary outcome variable, average early diastolic left ventricular relaxation velocity (E'), represents that average of values obtained from the basolateral and basal septal regions of the LV with an value of ≥8.5 cm/s used to define the lower limits of normal (Figure 1, main text).[2] Longitudinal strain measurements were made using commercially available speckle-tracking analysis software (Xcelera, Version

3.2.1.7-12-2011, Phillips Medical Systems, Netherlands).[3] Specifically, the highest-quality digital 2D apical 4-chamber view was selected for analysis. The endocardium was traced and a full thickness myocardial region of interest was selected. The software then automatically partitioned the LV into 6 segments including apical (n=2), septal (n=2), and lateral (n=2) territories and selected suitable speckles for tracking. The reliability of tracking was confirmed by the software's reliability parameter and by direct visual inspection to confirm appropriate systolic shortening. When either criterion suggested sub-optimal tracking efficiency, the endocardial trace and/or region of interest width were readjusted until an acceptable tracking score was obtained. By convention, longitudinal values are presented as negative numbers with lower (i.e. more negative) values representing greater systolic shortening. Measurements were obtained on 3 consecutive cardiac cycles and reported values represent a 3-cycle average. Resting heart rates represented the average values from the final 3 image loops of each participant's resting transthoracic echocardiographic assessment, a technique that ensured at least 15 minutes of quiet, uninterrupted physical inactivity.

Measurement Variability. The intraobserver and interobserver variability for LV mass and longitudinal strain were examined. Intraobserver variability was assessed by a single investigator using blinded assessment of 10 randomly selected subjects on 2 separate occasions. Interobserver variability was assessed in a group of 10 randomly selected subjects by 2 investigators blinded to each other's measurements and to study time point. Correlation coefficients for each measurement, derived from simple linear regression, were used to quantify variability with the following results: intraobserver LV mass (R^2= 0.946), intraobserver longitudinal strain (R^2= 0.968), interobserver LV mass (R^2= 0.921), and interobserver longitudinal strain (R^2= 0.972).

Coronary CT Angiography (CTA)

Image Acquisition. Participants had coronary CTA to assess for coronary artery plaque burden and calcification at the time of enrollment according to the guidelines of the Society of Cardiovascular Computed Tomography (SCCT).[4] Retrospectively ECG-gated CTA was performed on a dual-source 128-slice CT scanner (Definition Flash, Siemens Medical Systems, Erlangen, Germany). Prior to CTA, an 18 or 20 gauge antecubital intravenous (IV) catheter was placed. A brief interview prior to CT assessed for contraindications to metoprolol or nitroglycerin such as asthma or recent phosphodiesterase inhibitor use. Up to 20 mg of IV metoprolol was given in 5 mg aliquots at 5 minute intervals to achieve a hear rate of ≤65 beats per minute. A dose of 0.6 mg of sublingual nitroglycerin was given for coronary vasodilation. The CTA protocol included localizer images, a noncontrast ECG-gated high-pitch helical CT for assessment of coronary calcium, a test bolus of 20 cc IV contrast to time the proper delay for peak ascending aortic enhancement, and the CTA. All imaging was performed during an inspiratory breath hold; coverage included the heart from the diaphragm to the carina. For CTA 60-85 cc of iodinated IV contrast (iopamidol 370 g/cm3, Bracco Diagnostics, Princeton, NJ, USA) followed by a 40cc normal saline flush at a flow rate of 5 to 6 cc/second based on participant size was administered. The scan was performed with tube current modulation with a reference mAs of 370. Peak kilovoltage (kVp) was set to 120 for persons with a BMI ≥30 kg/m2 and 100 for <30 kg/m2. An adaptive pitch was used based on the heart rate, with a collimation of 128 x 0.6 mm and a rotation time of 280 ms. Noncontrast CT images were reconstructed with a slice thickness of 3 mm. CTA images were reconstructed with a slice thickness of 0.75 mm with a 0.4 mm overlap using a filtered back projection kernel at 5% intervals from 60-85% of the R-R interval for coronary evaluation, then again at a slice thickness of 1.5 mm without overlap at 5% intervals throughout the entire cardiac cycle. Image reconstruction was performed with a small

field of view of ≤20 cm to maximize spatial resolution. The cardiac phase or phases which minimized motion or other artifact were used for the analysis.

***Image Analysis*.** Image analysis was performed blinded to AAS use and all other clinical data on dedicated 3D workstations. The coronary artery calcium score (CACS) was calculated from the noncontrast images using the method of Agatston on a dedicated 3D workstation (MMWP, Siemens Medical Systems, Erlangen, Germany).[5] Coronary artery stenosis, the number of coronary artery segments with visible coronary plaque, and coronary artery plaque volume was assessed. Each participant's worst coronary artery stenosis was categorized as none, <25%, 25-49%, 50-69%, 70-99%, and 100% by visual inspection. Coronary plaque was defined as any discernable structure that could be assigned to the coronary artery wall on at least two orthogonal planes; the number of coronary artery segments with plaque was determined using a 17 segment model.[6] Semi-automated coronary plaque volume measurements were made using a second dedicated 3D workstation (AQi, Terarecon, Foster City, CA, USA). The workstation generated a centerline through the coronary artery lumen. The plaque length was established visually with markers at its proximal and distal extent. The inner luminal and outer wall coronary artery contours were automatically generated by the software and manually edited as necessary, and these voxels defined the coronary artery plaque volume in mm3. This volumetric technique for coronary plaque measurement has previously demonstrated excellent intra- and interobserver reproducibility.[7]

Appendix B – Supplementary Tables

Table 1: Demographic and Clinical Characteristics of Non-Anabolic-Androgenic-Steroid-Using Weightlifters and Non-Weightlifters.*

Characteristic	Non-AAS-Using Weightlifters (N = 54)	Non-Weightlifters (N = 50)
Demographic features		
Age, median (IQR), yr	43 (38–49)	43 (38-46)
Race, n (%) †		
White	41 (76)	45 (90)
Black	12 (22)	5 (10)
Asian	1 (2)	0
Ethnic background, n (%) †		
Not Hispanic	52 (96)	49 (98)
Hispanic	2 (4)	1 (2)
Anthropomorphic measures		
Height, median (IQR), m	1.8 (1.7-1.8)	1.8 (1.7-1.8)
Body surface area, median (IQR), m^2 ‡	2.2 (2.0–2.3)	2.0 (1.9–2.2)
Body mass index, median (IQR) §	29 (27-31)	26 (24-31)
Fat-free mass index, median (IQR) ‖	23 (21–25)	21 (19–22)
Exercise measures		
Time spent in aerobic exercise per week, n (%) #		
0-30 minutes	19 (35)	46 (92)
31-120 minutes	22 (41)	1 (2)
Greater than 120 minutes	13 (24)	3 (6)
Other potential cardiovascular risk factors		
Family history of coronary artery disease, n (%) **	12 (22)	12 (24)
Lifetime history of substance use, n (%)		
Regular cigarette smoking ††	19 (35)	18 (36)
Alcohol dependence ‡‡	7 (13)	4 (8)
Cocaine dependence ‡‡	5 (9)	5 (10)

* AAS indicates anabolic-androgenic steroids; IQR, interquartile range.

† Race and ethnic background were self-reported.

‡ By Mosteller formula.

§ The body mass index is the weight in kilograms divided by the square of the height in meters.

‖ The fat-free mass index is calculated as: $(W(1-BF)/H^2) + 6.1(1.8-H)$, where W = weight in kilograms, H = height in meters, and BF = percent body fat. (See reference 25 in the primary paper.)

Any self-reported aerobic exercise beyond ordinary daily activities.

** At least one first-degree relative reported to have had "coronary artery disease, angina, heart attack, angioplasty/stent, or coronary artery bypass surgery."

†† Any cigarette smoking beyond brief experimentation.

‡‡ By the Structured Clinical Interview for DSM-IV. (See reference 27 in the primary paper.)

Table 2. Echocardiographic Measures in Non-Anabolic-Androgenic-Steroid-Using Weightlifters and Non-Weightlifters.*

	Weightlifters	Non-Weightlifters	Weightlifters vs. Non-Weightlifters	
	Mean (SD)		Estimated difference	P value
Variable	(N = 54)	(N = 50)	(95% CI) †	
Primary outcomes				
Left ventricular ejection fraction, %	63 (8)	61 (6)	1.4 (-2.5 to 5.4)	0.47
Average early left ventricular relaxation velocity (E´), cm/s	11.1 (2.0)	11.4 (2.7)	0.2 (-0.9 to 1.4)	0.70
Secondary outcomes				
Longitudinal 4-chamber strain	-20 (3)	-20 (3)	0.4 (-1.3 to 2.0)	0.65
Early lateral left ventricular relaxation velocity (E´), cm/s	12.5 (2.3)	12.9 (3.5)	-0.2 (-1.7 to 1.4)	0.82
Early septal left ventricular relaxation velocity (E´), cm/s	9.8 (2.1)	9.8 (2.3)	0.6 (-0.5 to 1.7)	0.26
Left ventricular end diastolic internal diameter, cm	4.8 (0.5)	4.7 (0.4)	0.1 (-0.2 to 0.3)	0.45
Left ventricular end systolic internal diameter, cm	3.2 (0.4)	3.2 (0.50)	0.0 (-0.2 to 0.3)	0.79
Left ventricular end diastolic volume, mL	119 (28)	111 (23)	11 (-2 to 24)	0.11
Left ventricular end systolic volume, mL	45 (15)	43 (12)	2.7 (-4.3 to 9.8)	0.44
Interventricular septum thickness, cm	1.1 (0.1)	1.1 (0.2)	-0.0 (-0.1 to 0.1)	0.69
Posterior wall thickness, mm	1.1 (0.2)	1.0 (0.2)	0.12 (0.03 to 0.21)	0.007
Left ventricular mass, g	192 (40)	178 (47)	17 (-3 to 38)	0.10
Left ventricular mass/body surface area, g/m^2	89 (18)	86 (19)	8.3 (-1.6 to 18.1)	0.10
Left ventricular mass/height, g/m	107 (22)	100 (26)	11 (-1 to 22)	0.074
Left ventricular mass/height$^{2.7}$, g/m$^{2.7}$	40 (8)	38 (9)	4.5 (0.0 to 9.0)	0.050
Relative wall thickness	0.45 (0.08)	0.44 (0.09)	0.014 (-0.031 to 0.059)	0.55

* AAS indicates anabolic-androgenic steroids; CI, confidence interval.

† Estimated mean differences between groups, adjusted for age; race; family history of coronary artery disease; lifetime history of cocaine dependence, alcohol dependence, or regular tobacco use; aerobic exercise in the past 10 years; and body surface area by the Mosteller formula.

Table 3. Computed Tomography Coronary Angiography Findings in Non-Anabolic-Androgenic-Steroid-Using Weightlifters and Non-Weightlifters.*

Variable	Weightlifters (N = 53) Median (IQR)	Non-weightlifters (N = 48) Median (IQR)	Weightlifters vs Non-Weightlifters Mean difference in standardized ranks (95% CI) †	P Value
Primary outcome				
Plaque Volume, mm^3	0 (0-69)	13 (0-104)	-0.40 (-0.92 to 0.11)	0.12
Secondary outcomes				
Degree of stenosis for most severe stenosis ‡	0 (0-1)	1 (0-1)	-0.32 (-0.82 to 0.18)	0.21
Number of diseased coronary artery segments §	0 (0-1)	0.5 (0-1)	-0.30 (-0.80 to 0.20)	0.23
Agatston calcium score	0 (0-0.58)	0 (0-3.7)	-0.25 (-0.74 to 0.23)	0.30

* CI indicates confidence interval; IQR, interquartile range.

† Estimated mean difference between groups in rank, measured in standard deviation units, adjusted for age; race; family history of coronary artery disease; lifetime history of cocaine dependence, alcohol dependence, or tobacco use; and aerobic exercise in the past 10 years (see text).

‡ Represents the worst degree of stenosis of any coronary artery, on a scale of 0-4, where 0 = 0% stenosis; 1 = 1-25%; 2 = 26-49%; 3 = 50-69%; and 4 = 70-99%.

§ Represents the number of coronary artery segments showing any disease, with scores ranging from 0 to 10 diseased segments.

Table 4. Echocardiographic Findings in On-drug Anabolic-Androgenic Steroid Users, Off-drug Users, and Non-Users.*

	AAS Users			Non-Users	Comparisons †					
	Mean (SD)				On-drug AAS vs. non-users		Off-drug AAS vs. non-users		On-drug AAS vs. off-drug AAS	
Variable	All users (N = 86)	On-drug (N = 58)	Off-drug (N = 28)	(N = 54)	Estimated difference (95% CI)	P value	Estimated difference (95% CI)	P value	Estimated difference (95% CI)	P value
Primary outcomes										
Left ventricular ejection fraction, %	52 (11)	49 (10)	58 (10)	63 (8)	-13.6 (-17.3 to -9.8)	<0.001	-4.1 (-8.6 to 0.3)	0.072	-9.5 (-13.8 to -5.2)	<0.001
Early left ventricular relaxation velocity (E´), cm/s	9.3 (2.4)	8.9 (2.4)	10.1 (2.4)	11.1 (2.0)	-2.2 (-3.1 to -1.4)	<0.001	-1.1 (-2.2 to -0.1)	0.035	-1.1 (-2.1 to -0.1)	0.035
Secondary outcomes										
Global longitudinal strain, 4 chambers	-16 (4)	-14 (3)	-18 (4)	-20 (3)	5.8 (4.4 to 7.2)	<0.001	2.1 (0.4 to 3.9)	0.017	3.7 (2.0 to 5.3)	<0.001
Left ventricular relaxation velocity components, cm/s										
Lateral	10.6 (3.1)	10.2 (2.9)	11.4 (3.3)	12.5 (2.3)	-2.2 (-3.3 to -1.1)	<0.001	-1.1 (-2.4 to 0.3)	0.11	-1.1 (-2.4 to 0.2)	0.087
Septal	8.0 (2.2)	7.6 (2.2)	8.7 (1.9)	9.8 (2.1)	-2.2 (-3.1 to -1.4)	<0.001	-1.2 (-2.2 to -0.2)	0.021	-1.1 (-2.0 to -0.1)	0.031
Left ventricular internal diameter, cm										
End diastole	5.0 (0.6)	5.1 (0.7)	4.9 (0.5)	4.8 (0.5)	0.2 (-0.1 to 0.4)	0.18	0.00 (-0.3 to 0.3)	0.89	0.1 (-0.1 to 0.4)	0.30
End systole	3.6 (0.7)	3.6 (0.8)	3.6 (0.5)	3.2 (0.5)	0.3 (0.1 to 0.6)	0.015	0.2 (-0.1 to 0.5)	0.17	0.1 (-0.2 to 0.4)	0.49
Left ventricular volume, mL										
End diastole	125 (38)	129 (39)	118 (37)	119 (28)	3 (-10 to 16)	0.64	-8 (-23 to 8)	0.34	11 (-4 to 26)	0.16
End systole	61 (27)	67 (29)	49 (16)	45 (15)	19 (11 to 28)	<0.001	0.5 (-10 to 11)	0.93	19 (9 to 29)	<0.001
Interventricular septum thickness, cm	1.2 (0.2)	1.2 (0.2)	1.2 (0.2)	1.1 (0.1)	0.2 (0.1 to 0.3)	<0.001	0.2 (0.1 to 0.3)	<0.001	0.0 (-0.1 to 0.1)	0.92
Posterior wall thickness, cm	1.2 (0.2)	1.2 (0.2)	1.1 (0.2)	1.1 (0.2)	0.1 (0.1 to 0.2)	<0.001	0.00 (-0.0 to 0.1)	0.31	0.1 (0.0 to 0.2)	0.039
Left ventricular mass, g	245 (62)	253 (67)	228 (47)	192 (40)	52 (31 to 73)	<0.001	27 (2 to 52)	0.038	25 (1 to 49)	0.045
Left ventricular mass/body surface area, g/m^2	111 (61)	115 (30)	104 (20)	89 (18)	24 (15 to 34)	< 0.001	13 (1 to 25)	0.030	11 (0 to 23)	0.047
Left ventricular mass/height, g/m	138 (33)	143 (36)	129 (25)	107 (22)	31 (19 to 43)	<0.001	17 (3 to 31)	0.016	14 (0 to 27)	0.045
Left ventricular mass/height$^{2.7}$, g/m$^{2.7}$	52 (13)	54 (14)	49 (10)	40 (8)	13 (9 to 18)	<0.001	8.0 (3 to 13)	0.004	5 (-0 to 10)	0.052
Relative wall thickness	0.49 (0.11)	0.50 (0.12)	0.49 (0.11)	0.45 (0.08)	0.053 (0.013 to 0.093)	0.010	0.046 (-0.002 to 0.093)	0.061	0.007 (-0.039 to 0.053)	0.77

* AAS indicates anabolic-androgenic steroids; CI, confidence interval.

† Estimated mean differences between groups, adjusted for age; race; family history of coronary artery disease; lifetime history of cocaine dependence, alcohol dependence, or regular tobacco use; aerobic exercise in the past 10 years; and body surface area by the Mosteller formula.

Table 5. Comparison of Echocardiographic Findings in Anabolic-Androgenic Steroid Users and Non-Users Using Reduced and Augmented Sets of Covariate Adjustments.*

	AAS Users vs. Non-Users Comparisons with Reduced Set of Covariate Adjustments †		AAS Users vs. Non-Users Comparisons with Augmented Set of Covariate Adjustments ‡	
Variable	Estimated difference (95% CI)	P Value	Estimated difference (95% CI)	P Value
Primary outcomes				
Left ventricular ejection fraction, %	-10 (-14 to -7)	<0.001	-10 (-14 to -6)	<0.001
Average early left ventricular relaxation velocity (E´), cm/s	-1.9 (-2.7 to -1.1)	<0.001	-1.8 (-2.6 to -10.9)	<0.001
Secondary outcomes				
Longitudinal 4-chamber strain	4.7 (3.3 to 6.0)	<0.001	4.5 (3.1 to 5.9)	<0.001
Early lateral ventricular relaxation velocity (E´), cm/s	-1.9 (-2.9 to -0.9)	<0.001	-1.7 (-2.8 to -0.7)	0.001
Early septal ventricular relaxation velocity (E´), cm/s	-1.9 (-2.6 to -1.1)	<0.001	-1.8 (-25 to -1.0)	<0.001
Left ventricular end diastolic internal diameter, cm	0.1 (-0.1 to 0.3)	0.23	0.1 (-0.1 to 0.3)	0.32
Left ventricular end systolic internal diameter, cm	0.3 (0.1 to 0.5)	0.010	0.3 (0.1 to 0.5)	0.017
Left ventricular end diastolic volume, mL	0.7 (-11 to 13)	0.91	-0.2 (-12 to 12)	0.97
Left ventricular end systolic volume, mL	13 (5 to 21)	0.001	13 (4 to 21)	0.004
Interventricular septum thickness, cm	0.2 (0.1 to 0.2)	<0.001	0.2 (0.1 to 0.2)	<0.001
Posterior wall thickness, cm	0.1 (0.0 to 0.2)	<0.001	0.1 (0.0 to 0.2)	0.004
Left ventricular mass, g	46 (27 to 65)	<0.001	43 (22 to 63)	<0.001
Left ventricular mass/body surface area, g/m^2	22 (13 to 30)	< 0.001	20 (11 to 29)	< 0.001
Left ventricular mass/height, g/m	28 (18 to 39)	<0.001	26 (15 to 37)	<0.001
Left ventricular mass/$height^{2.7}$, $g/m^{2.7}$	12 (8 to 16)	<0.001	11 (7 to 15)	<0.001
Relative wall thickness	0.050 (0.015 to 0.087)	0.006	0.048 (0.011 to 0.086)	0.011

* AAS indicates anabolic-androgenic steroids; CI, confidence interval.

† Estimated mean difference between groups, adjusted only for age and race.

‡ Estimated mean difference between groups, adjusted for age; race; family history of coronary artery disease; lifetime history of cocaine dependence, alcohol dependence, or regular tobacco use; aerobic exercise in the past 10 years; hypertension (reported by history, OR showing current systolic pressure greater than 140 mm Hg OR diastolic pressure greater than 90 mm Hg at evaluation); and dyslipidemia (reported by history, OR showing low-density lipoprotein cholesterol greater than 160 mg/dL at evaluation).

Table 6. Comparison of Computed Tomography Coronary Angiography Findings in Anabolic-Androgenic Steroid Users and Non-Users Using Reduced and Augmented Sets of Covariate Adjustments.*

	AAS Users vs. Non-users Comparisons with Reduced Set of Covariate Adjustments †		AAS Users vs. Non-users Comparisons with Augmented Set of Covariate Adjustments ‡	
Variable	Mean difference in standardized ranks (95% CI)	P Value	Mean difference in standardized ranks (95% CI)	P Value
Primary outcome				
Plaque Volume, mm^3 §	0.44 (0.10 to 0.79)	0.012	0.41 (0.05 to 0.77)	0.028
Secondary outcomes				
Degree of stenosis for most severe stenosis ‖	0.37 (0.01 to 0.73)	0.046	0.30 (-0.08 to 0.68)	0.12
Number of diseased coronary artery segments #	0.35 (-0.01 to 0.71)	0.055	0.29 (-0.09 to 0.67)	0.13
Agatston calcium score §	0.16 (-0.17 to 0.50)	0.33	0.12 (-0.23 to 0.47)	0.49

* AAS indicates anabolic-androgenic steroids; CI, confidence interval.

† Estimated mean difference between groups in rank, measured in standard deviation units, adjusted only for age and race.

‡ Estimated mean difference between groups in rank, measured in standard deviation units, adjusted for age; race; family history of coronary artery disease; lifetime history of cocaine dependence, alcohol dependence, or regular tobacco use; aerobic exercise in the past 10 years; hypertension (reported by history, OR showing current systolic pressure greater than 140 mm Hg OR diastolic pressure greater than 90 mm Hg at evaluation); and dyslipidemia (reported by history OR showing low-density lipoprotein cholesterol greater than160 mg/dL at evaluation).

§ Four AAS users had received percutaneous coronary interventions, and thus their plaque volume and calcium score could not be quantified accurately. However, all 4 men showed extensive plaque as evidenced by their number of diseased segments and degree of stenosis for most severe stenosis. Therefore, for purposes of calculation, they were assigned the median values for plaque volume and calcium score, respectively, from among all study participants exhibiting nonzero plaque volume and calcium scores.

‖ Represents the worst degree of stenosis of any coronary artery, on a scale of 0-4, where 0 = 0% stenosis; 1 = 1-25%; 2 = 26-49%;3 = 50-69%; and 4 = 70-99%.

Represents the number of coronary artery segments showing any disease, with scores ranging from 0 to 10 diseased segments.

Table 7. Association of Computed Tomography Coronary Angiography Variables with Lifetime Duration of Anabolic-Androgenic Steroid Use Assessed With Reduced and Augmented Sets of Covariate Adjustments.*

	Reduced Set of Covariate Adjustments †		Augmented Set of Covariate Adjustments ‡	
Variable	Mean increase in standardized ranks (95% CI)	P Value	Mean increase in standardized ranks (95% CI)	P Value
Primary outcome				
Plaque volume, mm^3 §	0.60 (0.18 to 1.02)	0.005	0.58 (0.13 to 1.02)	0.011
Secondary outcomes				
Degree of stenosis for most severe stenosis ‖	0.69 (0.29 to 1.08)	< 0.001	0.64 (0.21 to 1.06)	0.004
Number of diseased coronary artery segments #	0.76 (0.35 to 1.18)	< 0.001	0.70 (0.26 to 1.14)	0.002
Agatston calcium score §	0.56 (0.16 to 0.96)	0.007	0.47 (0.03 to 0.90)	0.035

* AAS indicates anabolic-androgenic steroids; CI, confidence interval.

† Estimated increase in rank, measured in standard deviation units, for each 10-year increase in lifetime duration of AAS use, adjusted only for age and race.

‡ Estimated increase in rank, measured in standard deviation units, for each 10-year increase in lifetime duration of AAS use, adjusted for age; race; family history of coronary artery disease; lifetime history of cocaine dependence, alcohol dependence, or tobacco use; aerobic exercise in the past 10 years; hypertension (reported by history, OR showing current systolic pressure greater than 140 mm Hg OR diastolic pressure greater than 90 mm Hg at evaluation); and dyslipidemia (reported by history OR showing low-density lipoprotein cholesterol greater than 160 mg/dL at evaluation).

§ Four AAS users had received prior percutaneous coronary interventions, and thus plaque volume and calcium score could not be measured accurately in these men. However, all 4 of these men exhibited extensive plaque as evidenced by their number of diseased segments and degree of stenosis for most severe stenosis. Therefore, for purposes of calculation, they were assigned the median values for plaque volume and calcium score, respectively, from among all study participants exhibiting nonzero plaque volume and calcium scores.

‖ Represents the worst degree of stenosis of any coronary artery, on a scale of 0-4, where 0 = 0% stenosis; 1 = 1-25%; 2 = 26-49%; 3 = 50-69%;and 4 = 70-99%.

Represents the number of coronary artery segments showing any disease, with scores ranging from 0 to 10 diseased segments.

Appendix C – References

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