Cardiac and Metabolic Effects of Anabolic-Androgenic Steroid Abuse on Lipids, Blood Pressure, Left Ventricular Dimensions, and Rhythm

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Recent surveys and reports suggest that many athletes and bodybuilders abuse anabolic-androgenic steroids (AAS). However, scientific data on the cardiac and metabolic complications of AAS abuse are divergent and often conflicting. A total of 49 studies describing 1,467 athletes were reviewed to investigate the cardiovascular effects of the abuse of AAS. Although studies were typically small and retrospective, some associated AAS abuse with unfavorable effects. Otherwise healthy young athletes abusing AAS may show elevated levels of low-density lipoprotein and low levels of high-density lipoprotein. Although data are conflicting, AAS have also been linked with elevated systolic and diastolic blood pressure and with left ventricular hypertrophy that may persist after AAS cessation. Finally, in small case studies, AAS abuse has been linked with acute myocardial infarction and fatal ventricular arrhythmias. In conclusion, recognition of these adverse effects may improve the education of athletes and increase vigilance when evaluating young athletes with cardiovascular abnormalities. **(Am J Cardiol 2010; 106:893–901)**

Anabolic-androgenic steroids (AAS) are synthetic derivatives of testosterone that were originally developed in the late 1930s.[1] At present, the United States Food and Drug Administration has approved a variety of AAS to treat wasting syndrome in human immunodeficiency virus infection, hypogonadism, anemia accompanying renal and bone marrow failure, endometriosis, and cancer.[2,3] Unfortunately, AAS are frequently abused and have recently been linked to the tragic deaths of celebrated professional athletes in the United States.[4,5] Indeed, recent estimates suggest that >3 million individuals in the United States abuse AAS, including nandrolone decanoate, methandienone, stanozolol, androsterone, and androstane.[6,7] This rampant abuse led Congress to enact the Anabolic Steroids Control Act in 1990, requiring that anabolic steroids be added to Schedule 3 of the Controlled Substances Act.[8,9] All major professional sports organizations ban the use of AAS. Regardless, a recent report by Mitchell et al[10] showed that >29 major league baseball players tested positive for AAS abuse within the past 4 years. Many effects of AAS abuse are unclear. Although side effects are rare at therapeutic doses, abusers typically use 5 to 15 times the recommended clinical doses of AAS.[6,11,12] At such doses, general adverse effects include dose-dependent suppression of testicular function, gynecomastia, hepatotoxicity, and psychologic disorders.[6,11,12] Cardiac and metabolic effects of AAS abuse are particularly unclear, although there are alarming reports of cardiac morbidity and mortality. Moreover, athletes often abuse AAS for years, prolonging the potential for harm.[13–15] The purpose of this review is to synthesize the recent published reports on the cardiac and metabolic effects of AAS abuse in athletes.

Methods

We reviewed human studies retrieved from the PubMed, eMedicine, Heart Online, and Cochrane Databases in the English language. Inclusion terms were "anabolic steroid," "body builder," "athlete," and "steroid user," used alone or in combination with the terms "ventricular hypertrophy," "hypertension," "lipoprotein," "sudden death," "myocardial infarction" (MI), "cardiac," "arrhythmia," "tachycardia," and "fibrillation." The only exclusion term was "animal." In turn, a review of primary sources for each report was also conducted to find additional sources pertaining to their parent topics. Review of published reports was limited to the period from January 1, 1987, to December 31, 2009, because widespread testing became available in the United States and Europe at the end of 1986.

Results

We retrieved a total of 49 reports describing a total of 1,467 athletes (median 15 subjects/study). In aggregate, studies evaluated lipoprotein concentrations in 643 subjects, blood pressure in 348, left ventricular (LV) dimensions in 561, and sudden death in 102. We also report 4 key animal studies whose results shed insights into potential mechanisms linking AAS abuse with cardiovascular disease.

Clinical pharmacology of AAS: AAS include many agents with chemical structures derived from cholesterol that are synthesized in the liver and then metabolized in the

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Table 1
Effects of anabolic-androgenic steroid abuse on lipoprotein concentration

Study	Abused Agent	Dosage of AAS (mg/week)	Subjects, Age (years)			
			Users Ex-Users Controls	Users LDL (mg/dl) HDL (mg/dl)	Ex-users LDL (mg/dl) HDL (mg/dl)	Controls LDL (mg/dl) HDL (mg/dl)
Baldo-Enzi et al[39,¶]	Methenolone enanthate	100–300	14, 27 ± 5	129 ± 37	—	119 ± 17
	Testosterone cypionate	200–300	17, 25 ± 4	27 ± 11‖	—	48 ± 6
Fröhlich et al[40]	—	—	13, 27 ± 4	154 ± 58	—	121 ± 22
			11, 27 ± 7	23 ± 16‡	—	34 ± 7
Hartgens et al[41,¶]	Stanozolol	30–140	19, 31 ± 7	—	—	—
	Nandrolone decanoate	8–250	—	17 ± 9‖	—	47 ± 22
			16, 33 ± 5			
Lajarin et al[36]	Stanozolol	50–100	2, 27 ± 3	238 ± 8	—	—
	Methenolone enanthate	100	—	14 ± 0.4	—	—
			—			
Lane et al[42]	Testosterone	—	10, 26 ± 7	113 ± 27	86 ± 23	82 ± 12
	Nandrolone		8, 32 ± 7	27 ± 16†,‖	51 ± 16	51 ± 12
	Stanozolol		10, 24 ± 4			
Lenders et al[14,¶]	Methenolone	385–690	20, 26 ± 8	206 ± 21*,‡	156 ± 9	130 ± 13
	Testosterone	310–355	42, 28 ± 7	27 ± 3†,‖	42 ± 2	46 ± 2
	Oxymetholone	580–650	13, 28 ± 5			
McKillop and Ballantyne[37]	Stanozolol	280	8, 25 ± 4	243 ± 50‖	—	122 ± 27
	Nandrolone decanoate	200	—	16 ± 11‖	—	43 ± 12
			8, 25 ± 3			
Palatini et al[38,¶]	Testosterone enanthate and propionate	50–1,500	10, 27 ± 8	153 ± 34§	—	107 ± 41
	Stanozolol	50–150	—	30 ± 10	—	57 ± 13
			14, 28 ± 5			
Sader et al[13]	Stanozolol	—	10, 37 ± 3	—	—	—
	Nandrolone		—	23 ± 4‖	—	55 ± 4
	Creatine		10, 34 ± 3			
Urhausen et al[43]	Oral (i.e., mesterolone) and intramuscular AAS (i.e., stanozolol, nandrolone)	1,030	17, 31 ± 5	139 ± 37	119 ± 30	—
			15, 38 ± 7	17 ± 11†	43 ± 11	—
			—			
Zuliani et al[44]	Testosterone enanthate and propionate	750–1,500	6, 28 ± 2	—	—	—
			—	19 ± 8‖	—	49 ± 6
	Human growth hormone		8, 26 ± 2			

Data are expressed as ranges, numbers, or mean ± SD. The control group included bodybuilders who denied AAS abuse.
* $p < 0.05$ and † $p < 0.001$ versus ex-users; ‡ $p < 0.05$, § $p < 0.01$, and ‖ $p < 0.001$ versus controls.
¶ Other unspecified AAS abused.

adrenal glands and testes to AAS. Their structure resembles that of corticosteroids, explaining some similarities in actions in terms of renal sodium retention and hypertension.

The public health problem: prevalence of AAS abuse: AAS are abused by athletes primarily to increase lean muscle mass, enhance appearance, and improve performance.[16–18] Self-reported rates of abuse in bodybuilders range from 29% to 67%.[19–21] In a 1996 British survey of steroid abuse in competitive gymnasiums (albeit with few women), 29% of respondents admitted using AAS.[19] In an American study of 380 competitive bodybuilders in 1989, 54% of men and 10% of women admitted using AAS on a regular basis,[20] while 10 of 15 bodybuilders from an American power-lifting team admitted to taking AAS in a more recent study.[21]

Mortality in AAS abuse: the importance of cardiovascular causes: Mortality appears to be significantly higher in AAS abusers than in nonabusing athletes. In a retrospective case-cohort study of 248 AAS users and 1,215 controls (average age 23 years), 12 AAS users died during the study period,[22] providing a standard mortality ratio of 20.43 (95% confidence interval 10.56 to 35.70). Of the 1,215 athletes who did not abuse AAS, 22 died during the study period, resulting in a standard mortality ratio of 6.02 (95% confidence interval 3.77 to 9.12).[22] Although the exact causes of death were difficult to ascertain, a postmortem study of male Caucasian AAS abusers (aged 20 to 45 years) suggested primary cardiac pathology in 1/3,[23] while a recent case-control study[24,25] suggested cardiac causes in 2/3 of deaths, with others being attributed to suicide, hepatic coma, and malignancy. Many mechanisms have been proposed to explain potential adverse cardiovascular events of AAS.

Potential mechanisms: The physiologic and pharmacologic mechanisms of action of AAS on vascular structure and function are incompletely understood. AAS bind to