Prospective Echocardiographic Assessment of Androgenic-Anabolic Steroids Effects on Cardiac Structure and Function in Strength Athletes

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Abstract

Since the abuse of androgenic-anabolic steroids (AAS) has been associated with the occurrence of serious cardiovascular disease in young athletes, we performed two studies to investigate the effects of short-term AAS administration on heart structure and function in experienced male strength athletes, with special reference to dose and duration of drug abuse. In Study 1 the effects of AAS were assessed in 17 experienced male strength athletes (age 31 ± 7 y) who self-administered AAS for 8 or 12 – 16 weeks and in 15 non-using strength athletes (age 33 ± 5 y) in a non-blinded design. In Study 2 the effects of administration of nandrolone decanoate (200 mg/wk i. m.) for eight weeks were investigated in 16 bodybuilders in a randomised double blind, placebo controlled design. In all subjects M-mode and two-dimensional Doppler-echocardiography were performed at baseline and after 8 weeks AAS administration. In the athletes of Study 1 who used AAS for 12 – 16 weeks a third echocardiogram was also made at the end of the AAS administration period. Echocardiographic examinations included the determination of the aortic diameter (AD), left atrium diameter (LA), left ventricular end diastolic diameter (LVEDD), interventricular septum thickness (IVS), posterior wall end diastolic wall thickness (PWEDWT), left ventricular mass (LVM), left ventricular mass index (LVMI), ejection fraction (EF) and right ventricular diameter (RVD). For assessment of the diastolic function measurements of E and A peak velocities and calculation of E/A ratio were used. In addition, acceleration and deceleration times of the E-top (ATM and DT, respectively) were determined. For evaluation of factors associated with stroke volume the aorta peak flow (AV) and left ventricular ejection times (LVET) were determined. In Study 1 eight weeks AAS self-administration did not result in changes of blood pressure or cardiac size and function. Additionally, duration of AAS self-administration did not have any impact on these parameters. Study 2 revealed that eight weeks administration of nandrolone decanoate did not induce significant alterations in blood pressure and heart morphology and function. Short-term administration of AAS for periods up to 16 weeks did not lead to detectable echocardiographic alterations of heart morphology and systolic and diastolic function in experienced strength athletes. The administration regimen used nor the length of AAS abuse did influence the results. Moreover, it is concluded that echocardiographic evaluation may provide incomplete assessment of the actual cardiac condition in AAS users since it is not sensitive enough to detect alterations at the cellular level. Nevertheless, from the present study no conclusions can be drawn of the cardiotoxic effects of long term AAS abuse.

Key words
Androgenic-anabolic steroids · nandrolone decanoate · echocardiography · blood pressure · heart morphology · heart function · doping

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Introduction

Nowadays many people perform resistance training to improve their physical and mental health status or for esthetical purposes. Most people try to reach their goals with resistive training programs solely, but an increasing number uses performance enhancing substances for more and faster improvements [38]. Androgenic-anabolic steroids (AAS) have become very popular among strength athletes, especially because of their muscle building properties and the widespread availability on the black market [14,38]. The hazardous effects of these drugs on health status are of great concern since these athletes self-administer supratherapeutical doses and the quality of the substances purchased on the black market is not guaranteed [10,14]. Recently, the detrimental side-effects of AAS abuse, including liver disease [9,12], malignant tumors [23], dysfunction of the reproductive system [9,15], and alterations of the mental state and behaviour [2,15,23] have been reviewed in the literature thoroughly. Moreover, in recent years these substances have been associated with the occurrence of serious cardiovascular disease in healthy, young athletes [8,11,13,18,21,31]. Although these reports are of great concern, until now scientific data about a relationship between AAS administration and heart disease in humans is equivocal [15,23]. In this light, several researchers have investigated the effects of AAS on blood pressure and heart morphology and function. However, both cross-sectional and longitudinal studies were not able to report conclusive evidence. Some investigations observed (slight) alterations of cardiac morphology or function [7,16,27,36,37], whereas others did not [6,22,28,29,35,39]. Summarizing the available research data, they do not support unequivocally whether AAS induce detrimental effects on the heart in humans. Therefore, the purpose of this study was to investigate the effects of AAS on heart structure and function in experienced strength athletes. Our main objectives were to study:

1. the effects of the administration of a single anabolic steroid and of polydrug regimens on heart morphology and function, and
2. the impact of duration of AAS self-administration on heart morphology and function.

Material and Methods

Subjects

This study was part of a larger study exploring the effects of androgenic-anabolic steroids abuse on body composition and health status in strength athletes. To meet the study objectives, we recruited a large number of volunteers by flyers in regional gym clubs. In several meetings the volunteers were extensively informed about the study objectives and approach. Approximately 90 strength athletes applied for participation in one or more of these studies. The subjects had to answer an extensive questionnaire with questions related to current and previous health status, training habits and history, dietary intake and use of nutritional supplements, and the use of AAS. In a personal interview with a medical doctor (F.H.) the completed questionnaires were discussed. Moreover, all subjects underwent a full medical examination for evaluation of their health status and to exclude any relevant disease conditions. Only volunteers who appeared to be healthy and who met all inclusion and exclusion criteria set by the investigators were admitted to the study. Inclusion criteria were: male, strength training experience for a minimum of 3 y, at least 4 strength training work outs per week or 8 h strength training weekly, and age between 20 and 45 years. The following exclusion criteria were set: hypertension, diabetes mellitus, liver disease or abnormal liver enzyme serum levels, hereditary hypercholesterolaemia, elevated serum total cholesterol (> 6.5 mmol/l), infertility and smoking.

Table **1** Physical and training characteristics of the strength athletes

	AAS (n = 17)	*Controls (n = 15)*
Study 1		
Age (years)	32 ± 7	33 ± 5
Height (cm)	176 ± 9	177 ± 7
Body weight (kg)	84.9 ± 10.2	87.7 ± 11.1
Percentage fat (%)	16.7 ± 5.2	19.5 ± 3.7
Training load (hours/week)	8.7 ± 2.6	8.3 ± 2.4
Training experience (years)	10.7 ± 7.4	8.8 ± 3.8
	ND-group (n = 9)	*PLAC-group (n = 7)*
Study 2		
Age (years)	33 ± 9	31 ± 9
Height (cm)	175 ± 10	177 ± 7
Body weight (kg)	76.0 ± 12.1	83.8 ± 9.0
Percentage fat (%)	15.3 ± 2.6	17.6 ± 2.4
Training load (hours/week)	7.4 ± 2.	9.1 ± 2.0
Training experience (years)	7.3 ± 2.1	6.4 ± 2.8

The study was approved by the Medical Ethical Review Committee of the Maastricht University and the University Hospital Maastricht, and all subjects gave their written informed consent before participating.

Study design

To meet the purpose of this investigation, we designed two studies that were considered to be complementary.

Study 1

This study was conducted to investigate the effects of self-administration of high doses AAS on heart morphology and function as well as to explore the impact of duration of AAS use in 32 strength athletes. Seventeen strength athletes who intended to start self-administration of AAS participated in this study (AAS group) and the control group (Controls) consisted of 15 non-using strength athletes. Physical and training characteristics of both groups are presented in Table **1**.

Most participants (n = 26) performed resistive training mainly for esthetical purposes. Two strength athletes carried out strength training for esthetical reasons as well as part of their boxing training. The remaining four athletes were mainly involved in power lifting training and competition.

The controls did not have any experience in AAS use. On the other hand, all participants of the AAS group had self-administered AAS before. They had started the administration of these substances on average 4.6 years before (range 1 to 14 years). These

subjects used on average 2 cycles per year and the mean number of AAS cycles used was 6.7 (range 1 to 30 cycles).

Before entering the study all volunteers were expected to be free of AAS use for at least three months. Information obtained from the subjects indicated that the mean AAS withdrawal period was 7.8 months (range 3 to 30 months). To exclude recent AAS use objectively, in all subjects (AAS group and Controls) urine samples were collected for drug analysis before entering the study.

The strength athletes purchased the drugs mainly on the black market although some had received a prescription from a medical doctor. AAS courses were composed on their own insights and beliefs. The investigators were not involved in providing AAS, no attempt was made to influence the choice of the AAS used nor did the researchers play any role in AAS administration. In Table **2** an outline of the AAS used, route of administration and dose for each subject is given.

In all subjects echocardiographic measurements were performed before the start of the study and after eight weeks of strength training with or without concomitant AAS self-administration (AAS group and Controls, respectively). In addition, since part of the AAS users had decided to self-administer AAS for 12 to 16 weeks, in these strength athletes echocardiographic measurements were also performed at the end of the AAS course.

Study 2

This study was designed to investigate the effects of the administration of a single, very popular anabolic steroid, nandrolone decanoate (Deca-Durabolin®, Organon BV, Oss, The Netherlands), on heart morphology and function in a randomized, double blind and placebo controlled design. Sixteen well-trained recreational bodybuilders volunteered for this study. They were randomly assigned to the nandrolone decanoate or placebo group (ND or PLAC, respectively). In both groups two subjects had previous experience with AAS administration, whereas the remainder had never used such substances before. Physical and training characteristics are presented in Table **1**.

Once a week the bodybuilders visited the laboratory for administration of the intramuscular injection containing either 200 mg/week nandrolone decanoate or placebo for eight weeks. The injections were administered by one of the investigators (F.H.). The echocardiographic measurements were performed at baseline and after eight weeks study period.

Blood pressure measurements

After a resting period of 5 minutes in supine position, systolic and diastolic blood pressure were measured with a sphygmomanometer. In both studies, measurements were performed at baseline and after eight weeks.

Echocardiographic measurement

M-mode and two-dimensional Doppler-echocardiography using a Hewlett-Packard Sonos 2500 ultrasound system with standard imaging transducers was performed in all subjects. To avoid inter-observer variability, all echocardiographic measurements were made by the same experienced echocardiographer (E.C). Measured were aortic diameter (AD), left atrium diameter (LA), left ventricular end diastolic diameter (LVEDD), interventricular septum thickness (IVS), posterior wall end diastolic wall thickness (PWEDWT), left ventricular mass (LVM), left ventricular mass index (LVMI), ejection fraction (EF) and right ventricular diameter (RVD). Evaluation of diastolic function was performed by measuring E and A peak velocities and calculation of E/A ratio. In addition, acceleration and deceleration times of the E-top (ATM and DT, respectively) were measured. For evaluation of factors associated with stroke volume the aorta peak flow (AV) and left ventricular ejection times (LVET) were determined.

Monitoring training, nutrition and compliance

All participants were asked to maintain their regular training and nutritional habits. To monitor these habits, the nutritional intake was determined by means of a three day diary and the training data were obtained by a one week log book. From all subjects of study 1 and 2 the dietary and training data were collected just before the start of the study and in week 8. In the AAS users who self-administered AAS for 12 to 16 weeks (study 1) these data were also obtained in the last week of AAS use.

Throughout the study period in all subjects several urine samples were collected for drug analysis to objectively exclude recent drug use. The subjects of study 1 provided urine samples at baseline and after 8 weeks. In the athletes who self-administered AAS for 12 to 16 weeks another urine sample was collected at the end of the drug administration period. The participants of study 2 provided urine samples at baseline and after 4 and 8 weeks study period. From the urine samples of both studies approximately one third was randomly selected for analysis by the Netherlands Institute for Drug and Doping Research (NIDDR), Utrecht (The Netherlands) to detect metabolites of anabolic agents.

Statistical analysis

All data are presented as mean and standard deviations (mean ± sd). In both studies comparison of baseline data between groups were performed with the Mann-Whitney U-test. In the non-blinded investigation (study 1) the same test was applied for analysis of the intervention effects. We compared changes in the AAS group after eight weeks of drug administration with the alterations in the Control group. The impact of duration of AAS self-administration was analyzed by comparing the changes at the end of the drug administration period between the short-term and long-term users. In the double blind study (study 2) the intervention effects were analyzed using ANCOVA since several echocardiographic data of ND and PLAC at baseline differed significantly. In all analyses the level of significance was set at $p < 0.05$.

Results

Study 1

At baseline both groups were comparable with respect to the physical characteristics, training and nutritional data, as well as blood pressure and echocardiographic data. In the AAS group no significant alterations in blood pressure (Table **3**) and the echocardiographic assessment of heart morphology and function could be observed after 8 weeks of AAS administration (Table **4**). Furthermore, analyzing the impact of duration of AAS self-ad-

Table **2** Outline of the AAS used, dosages and route of administration in the subjects of study 1

No.	*ID*	*Duration AAS use*	*AAS used and route of administration*	*Generic names*	*Total amount of drugs used*
1.	BC101	16 weeks	Stromba (i. m.)	Stanozolol	500 mg
			Deca-Durabolin (i. m.)	Nandrolone decanoate	350 mg
			Primobolan (p. o.)	Metenolone	375 mg
			Primobolan (i. m.)	Metenolone	1400 mg
			Masteron (p. o.)	Drostanolone	14 mg
			Proviron (p. o.)	Mesterolone	350 mg
2.	SS102	16 weeks	Stromba (i. m.)	Stanozolol	500 mg
			Deca-Durabolin (i. m.)	Nandrolone deconoate	350 mg
			Primobolan (p. o.)	Metenolone	375 mg
			Primobolan (i. m.)	Metenolone	1400 mg
			Masteron (p. o.)	Drostanolone	14 mg
			Proviron (p. o.)	Mesterolone	350 mg
3.	MB108	8 weeks	Deca-Durabolin (i. m.)	Nandrolone decanoate	1600 mg
			Parabolan (i.m)	Trenbolone acetate	228 mg
			Dianabol (p. o.)	Methandrostenolone	940 mg
			Pregnyl (i. m.)	Choriongonadotrophine	9000 IU
4.	JD111	12 weeks	Testoviron (i. m.)	Testosterone enanthate	1250 mg
			Strombaject (i. m.)	Stanozolol	700 mg
			Decadurabolin (i. m.)	Nandrolone decanoate	100 mg
5.	ES112	16 weeks	Strombaject (i. m.)	Stanozolol	750 mg
			Stromba (p. o.)	Stanozolol	450 mg
			Omnadren (i. m.)	Testosterone propionate	375 mg
			Deca-Durabolin (i. m.)	Nandrolone decanoate	875 mg
			Primobolan (i. m.)	Metenolone	300 mg
6.	JN113	8 weeks	Dianabol (p. o.)	Methandrostenolone	960 mg
			Deca-Durabolin (i. m.)	Nandrolone decanoate	300 mg
			Masteron (i. m.)	Drostanolone	300 mg
7.	GS115	16 weeks	Clenbuterol (p. o.)	Clenbuterol	This subject used the listed drugs in a stacking way from the start, but did not know the doses used. He qualified them as “high”.
			Winstrol (p. o.)	Stanozolol	
			Deca-Durabolin (i. m.)	Nandrolone decanoate	
			Stromba (p. o.)	Stanozolol	
			Stromba (i. m.)	Stanozolol	
			Parabolan (i. m.)	Trenbolone acetate	
			Pregnyl (i. m.)	Choriongonadotrophine	
			Undestor (i. m.)	Testosterone undecanoate	
			Nolvadex (p. o.)	Tamoxiphene	
8.	FB121	8 weeks	Deca-Durabolin (i. m.)	Nandrolone decanoate	2000 mg
			Strombaject (i. m.)	Stanozolol	750 mg
			Pregnyl (i. m.)	Choriongonadotrophine	13500 IU
9.	RT122	16 weeks	Stromba (p. o.)	Stanozolol	1080 mg
			Dianabol (p. o.)	Methandrostenolone	1240 mg
			Testosterone (i. m.)	Testosterone heptilate	3000 mg
10.	GR124	8 weeks	Dianabol (p. o.)	Methandrostenolone	560 mg
			Proviron (p. o.)	Mesterolone	1400 mg
			Primobolan (i. m.)	Metenolone	800 mg
			Deca-Durabolin (i. m.)	Nandrolone decanoate	400 mg
			Sustanon (i. m.)	Testosterone (phenyl-)propionate/ isohexanoate	1750 mg
			Parabolan (i. m.)	Trenbolone acetate	602 mg
			Strombaject (i. m.)	Stanozolol	250 mg
			Boldane (i. m.)	Boldenone	300 mg
			Stromba (p. o.)	Stanozolol	420 mg
11.	PW125	8 weeks	Proviron (p. o.)	Mesterolone	5600 mg
			Primobolan (i. m.)	Metenolone	1600 mg
12.	MD139	12 weeks	Synasteron (p. o.)	Oxymetenolone	3500 mg
			Deca-Durabolin (i. m.)	Nandrolone decanoate	1625 mg
13.	FL151	12 weeks	Stromba (p. o.)	Stanozolol	1036 mg
			Stromba (i. m.)	Stanozolol	850 mg
			Testoviron (i. m.)	Testosterone enanthate	3750 mg
			Testex Leo (i. m.)	Testosterone cypionate	5000 mg
			Pregnyl (i. m.)	Choriongonadotrophine	4500 IU
14.	HK401	8 weeks	Dianabol (p. o.)	Methandrostenolone	1115 mg
			Primobolan (p. o.)	Metenolone	1850 mg
			Proviron (p. o.)	Mesterolone	675 mg
15.	GT402	16 weeks	Stromba (p. o.)	Stanozolol	2170 mg
			Anapolon (p. o.)	Oxymetholone	1225 mg

continued on next page

Table **2** *Continuation*

No.	*ID*	*Duration AAS use*	*AAS used and route of administration*	*Generic names*	*Total amount of drugs used*
16.	DV403	8 weeks	Deca-Durabolin (i. m.)	Nandrolone decanoate	4400 mg
			Spiropent (p. o.)	Clenbuterol	1.68 mg
			Testoviron (i. m.)	Testosterone enanthate	2500 mg
			Testex Leo (i. m.)	Testosterone cypionate	1000 mg
			Masteron (i. m.)	Drostanolone	300 mg
			Strombaject (i. m.)	Stanozolol	1200 mg
17.	EK404	12 weeks	Strombaject (i. m.)	Stanozolol	1150 mg
			Testosterone (i. m.)	Testosterone	5500 mg
			Spiropent (p. o.)	Clenbuterol	1.00 mg
			Anadrol (p. o.)	Oxymetholone	1900 mg
			Pregnyl (i. m.)	Choriongonadotrophine	1500 IU
			Nolvadex (p. o.)	Tamoxiphene	440 mg

Table **3** Systolic and diastolic blood pressure measurements at baseline and after 8 weeks in both studies

		Baseline	*8 weeks*
Study 1			
Systolic blood pressure (mmHg)	AAS	131 ± 12	139 ± 13
	Controls	129 ± 14	134 ± 8
Diastolic blood pressure (mmHg)	AAS	83 ± 6	85 ± 12
	Controls	81 ± 9	81 ± 7
Study 2			
Systolic blood pressure (mmHg)	ND-group	133 ± 16	128 ± 16
	PLAC-group	130 ± 14	123 ± 5
Diastolic blood pressure (mmHg)	ND-group	83 ± 13	80 ± 7
	PLAC-group	84 ± 6	78 ± 10

Table **4** Echocardiographic measurements at baseline and after 8 weeks in the non-blinded study (study 1)

		Baseline	*8 weeks*
AD (mm)	AAS	34.2 ± 3.3	34.1 ± 3.4
	Controls	33.9 ± 3.5	33.9 ± 3.3
LA (mm)	AAS	41.2 ± 3.6	41.7 ± 3.7
	Controls	42.5 ± 3.5	41.8 ± 3.7
LVEDD (mm)	AAS	53.6 ± 5.1	53.4 ± 4.6
	Controls	53.5 ± 4.3	53.2 ± 3.9
IVS (mm)	AAS	8.6 ± 0.9	8.8 ± 1.1
	Controls	8.4 ± 0.9	8.3 ± 1.0
PWEDWT (mm)	AAS	8.9 ± 0.9	8.9 ± 0.7
	Controls	8.6 ± 0.8	8.6 ± 0.8
EF (%)	AAS	63.4 ± 5.0	62.8 ± 4.7
	Controls	63.1 ± 4.2	60.9 ± 4.9
LVM (gram)	AAS	215.1 ± 43.8	216.4 ± 43.3
	Controls	207.3 ± 46.1	206.0 ± 44.6
LVMI(gram/m^2)	AAS	108.0 ± 22.3	104.2 ± 17.0
	Controls	100.9 ± 20.1	100.5 ± 20.6
AV (mm/sec)	AAS	138.8 ± 24.0	147.2 ± 33.7
	Controls	145.5 ± 30.5	139.4 ± 30.8
LVET (msec)	AAS	285.0 ± 24.2	278.8 ± 28.3
	Controls	292.0 ± 22.5	297.3 ± 14.9
ATM (msec)	AAS	96.0 ± 21.0	100.0 ± 20.9
	Controls	100.0 ± 23.2	100.0 ± 18.9
DT (msec)	AAS	164.0 ± 31.8	174.7 ± 34.7
	Controls	174.1 ± 28.1	162.0 ± 38.4
E/A ratio	AAS	1.51 ± 0.44	1.41 ± 0.41
	Controls	1.71 ± 0.71	1.83 ± 0.52
RVD (cm)	AAS	3.6 ± 0.4	3.6 ± 0.4
	Controls	3.4 ± 0.4	3.5 ± 0.4

Aortic diameter (AD), left atrium diameter (LA), left ventricular end diastolic diameter (LVEDD), interventricular septum thickness (IVS), posterior wall end diastolic wall thickness (PWEDWT), left ventricular mass (LVM), left ventricular mass index (LVMI), ejection fraction (EF), ratio between E-top velocity and A-top velocity (E/A ratio), acceleration times of the E-top (ATM), deceleration times of the E-top (DT), aorta flow velocity (AV), left ventricular ejection times (LVET), right ventricular diameter (RVD).

ministration did not reveal any difference between short-term and long-term use (Table **5**).

Study 2

At baseline the physical characteristics, training and nutritional data, blood pressure and most echocardiographic measurements were comparable between groups. Echocardiographic determination of LVEDD and LVM, however, were significantly different between both groups at the start. Eight weeks administration of nandrolone decanoate did not induce significant alterations in blood pressure (Table **3**) and echocardiographic measurements of heart morphology nor in parameters reflecting systolic and diastolic cardiac function (Table **6**).

Discussion

Main observations

The main finding of the present investigation was that the short-term administration of AAS did not affect blood pressure, heart structure and cardiac function of strength athletes as determined by echocardiography. Since both studies are complementary, the absence of detectable alterations indicates that heart structure and systolic as well as diastolic function is not dependent on the regimen or dose of the AAS used with respect to administration periods for up to 16 weeks.

Table **5** Impact of duration of AAS self-administration on echocardiographic measurements: short-term (n = 10) vs long-term (n = 7) AAS administration

		Baseline	*End AAS course*
AD (mm)	Short-AAS	34.4 ± 3.7	34.7 ± 4.1
	Long-AAS	33.9 ± 2.9	34.4 ± 2.6
LA (mm)	Short-AAS	41.0 ± 3.4	41.0 ± 3.0
	Long-AAS	41.5 ± 4.0	41.6 ± 4.6
LVEDD (mm)	Short-AAS	53.6 ± 6.7	52.6 ± 5.8
	Long-AAS	53.6 ± 3.0	54.1 ± 3.1
IVS (mm)	Short-AAS	8.9 ± 0.8	9.1 ± 1.2
	Long-AAS	8.4 ± 0.9	8.5 ± 0.8
PWEDWT (mm)	Short-AAS	9.0 ± 0.9	9.2 ± 0.7
	Long-AAS	8.8 ± 0.9	8.9 ± 0.6
EF (%)	Short-AAS	63.4 ± 5.0	63.8 ± 5.2
	Long-AAS	63.4 ± 5.4	62.6 ± 4.1
LVM (gram)	Short-AAS	221.4 ± 55.1	221.9 ± 54.9
	Long-AAS	207.9 ± 28.3	214.9 ± 25.6
LVMI(gram/m^2)	Short-AAS	114.9 ± 26.4	112.1 ± 22.4
	Long-AAS	100.2 ± 14.5	101.3 ± 11.0
AV (mm/sec)	Short-AAS	144.3 ± 30.5	155.3 ± 43.9
	Long-AAS	132.5 ± 12.9	131.5 ± 12.2
LVET (msec)	Short-AAS	278.8 ± 21.7	273.3 ± 33.5
	Long-AAS	291.3 ± 26.4	286.3 ± 22.6
ATM (msec)	Short-AAS	104.4 ± 28.8	100.0 ± 24.0
	Long-AAS	95.0 ± 15.1	102.5 ± 13.9
DT (msec)	Short-AAS	168.9 ± 29.8	180.0 ± 33.5
	Long-AAS	160.0 ± 26.7	168.8 ± 43.6
E/A ratio	Short-AAS	1.51 ± 0.49	1.35 ± 0.50
	Long-AAS	1.51 ± 0.40	1.56 ± 0.35
RVD (cm)	Short-AAS	3.6 ± 0.4	3.6 ± 0.4
	Long-AAS	3.6 ± 0.3	3.7 ± 0.3

Aortic diameter (AD), left atrium diameter (LA), left ventricular end diastolic diameter (LVEDD), interventricular septum thickness (IVS), posterior wall end diastolic wall thickness (PWEDWT), left ventricular mass (LVM), left ventricular mass index (LVMI), ejection fraction (EF), ratio between E-top velocity and A-top velocity (E/A ratio), acceleration times of the E-top (ATM), deceleration times of the E-top (DT), aorta flow velocity (AV), left ventricular ejection times (LVET), right ventricular diameter (RVD).

Table **6** Echocardiographic measurements at baseline and after 8 weeks in the double blind, placebo controlled study (study 2)

		Baseline	*8 weeks*
AD (mm)	ND-group	32.1 ± 2.8	32.2 ± 2.7
	PLAC-group	33.9 ± 2.1	33.3 ± 2.4
LA (mm)#	ND-group	39.6 ± 4.4	39.9 ± 4.0
	PLAC-group	43.7 ± 2.1	42.9 ± 3.4
LVEDD (mm)##	ND-group	49.8 ± 3.2	50.0 ± 2.0
	PLAC-group	53.3 ± 2.3	52.9 ± 2.0
IVS (mm)	ND-group	8.0 ± 0.9	7.9 ± 0.8
	PLAC-group	8.3 ± 0.5	8.1 ± 0.8
PWEDWT (mm)	ND-group	8.4 ± 0.7	8.3 ± 0.7
	PLAC-group	8.9 ± 0.4	8.7 ± 0.5
EF (%)	ND-group	63.8 ± 3.2	63.0 ± 5.6
	PLAC-group	62.7 ± 3.8	61.6 ± 5.8
LVM (gram)#	ND-group	174.7 ± 32.7	172.7 ± 29.9
	PLAC-group	205.7 ± 17.0	198.3 ± 14.2
LVMI (gram/m^2)	ND-group	90.2 ± 12.7	89.1 ± 10.3
	PLAC-group	101.9 ± 8.4	98.9 ± 9.5
AV (mm/sec)	ND-group	136.9 ± 20.6	128.9 ± 10.7
	PLAC-group	138.0 ± 19.3	139.9 ± 9.3
LVET (msec)	ND-group	275.6 ± 24.0	227.8 ± 13.9
	PLAC-group	290.0 ± 10.0	280.0 ± 18.3
ATM (msec)	ND-group	84.4 ± 12.4	100.0 ± 17.3
	PLAC-group	97.1 ± 13.8	90.0 ± 16.3
DT (msec)	ND-group	159.0 ± 31.6	152.2 ± 26.8
	PLAC-group	158.6 ± 27.9	158.6 ± 13.5
E/A ratio	ND-group	1.57 ± 0.52	1.69 ± 0.48
	PLAC-group	1.68 ± 0.44	1.66 ± 0.26
RVD (cm)	ND-group	3.2 ± 0.3	3.5 ± 0.5
	PLAC-group	3.6 ± 0.3	3.6 ± 0.3

Aortic diameter (AD), left atrium diameter (LA), left ventricular end diastolic diameter (LVEDD), interventricular septum thickness (IVS), posterior wall end diastolic wall thickness (PWEDWT), left ventricular mass (LVM), left ventricular mass index (LVMI), ejection fraction (EF), ratio between E-top velocity and A-top velocity (E/A ratio), acceleration times of the E-top (ATM), deceleration times of the E-top (DT), aorta flow velocity (AV), left ventricular ejection times (LVET), right ventricular diameter (RVD).
means significant ($p < 0.10$) difference between both groups at the start
means significant ($p < 0.05$) difference between both groups at the start

Baseline echocardiographic measurements

In all subjects of both studies, the hearts showed enlargement of the left ventricle and left ventricle wall thickness, but all measurements were within the limits of physiologic adaptation as proposed by Pellicia and coworkers [24,30]. In both studies, left ventricular mass ranged from 132 to 309 grams and the left posterior wall thickness of the several strength athletes exceeded the normal range of males. In such cases it is mandatory to examine for a heart disease condition. However, in the absence of abnormal left ventricle filling, no decrement of the left ventricular cavity and a normal left ventricular hypertrophy pattern, which were appropriate in all subjects, such cardiac enlargements can be attributed to vigorous and demanding training regimens rather than a heart disease condition [24,34]. Finally, at baseline all subjects were considered to have normal echocardiographic examinations without any detrimental effect due to previous AAS use.

Effects of AAS administration

The present study showed that the administration of a high dose of nandrolone decanoate for 8 weeks did not affect cardiac structure and function as determined by echocardiography. The same applied for the use of high dosages of AAS polydrug regimens for 8 weeks as well as for such courses up to 16 weeks.

Several cross-sectional studies reported larger posterior wall thickness, interventricular septum thickness and/or the left ventricular mass in AAS using athletes compared to their non-using counterparts [7,16,27,36,37]. However, other investigators were unable to detect differences in cardiac dimensions between steroid users and non-users [6,22,28,35,39]. Only a few of these studies examined heart function, one reporting an impairment of diastolic function [36], while another did not [7]. The discrepancies observed in the study outcome may be mainly attributable to confounding factors (especially, selection of subjects) rather than to steroid use. Our suggestion is enforced by the more con-

sistent results of longitudinal studies. All longitudinal studies, except one [27], failed to demonstrate changes of heart structure and function due to the administration of high doses of AAS for short periods [6,22,29,39]. Only one study registered increments of the left ventricular end diastolic diameter (LVEDD), the thickness of the interventricular septum (IVS) and the left ventricular mass (LVM) during steroids use [27]. However, it is noteworthy to mention that the subjects in that study trained more frequently (6.5 vs 5.0 sessions per week) and heavier (3.6 vs 2.7 heavy sessions per week) when on steroids compared to the period off steroids. Moreover, it is well known that detraining may induce a marked reduction of the training induced cardiac adaptations within a short time period [24]. Therefore, in our opinion the findings by Sachtleben and coworkers remain debatable whether the cardiac alterations may be attributed to short-term AAS administration rather than to the training alterations.

Unfortunately, no studies are available that investigated the long-term effects of AAS on heart structure and function. Nevertheless, the increase of reports indicating detrimental long term cardiotoxic effects of AAS are of great medical concern.

AAS and animal hearts

Although echocardiographic studies in human subjects may indicate that the side-effects of AAS on the heart structure seem to be limited, it has been well established in animal studies that these doping agents posses the potential to affect the heart. There is solid evidence available that the administration of testosterone or anabolic steroids leads to cardiomegaly in animals [5,19,20,25,26]. Such adaptations have been documented within a few weeks after starting AAS administration [19,26], but might be reversible after cessation [25]. Furthermore, steroids have been demonstrated to exert detrimental effects at the cellular level of animal hearts [1,3,32]. A direct hazardous effect on the mitochondria may lead to membranous defects and disturb the integrity of these cell substances [3,4]. Myofibrils may show disintegration or widened and twisted Z-bands or even complete dissolution of the sarcomeric units. Additionally, an increase of nonmyofibrillar filaments was found due to anabolic steroid administration [3,4]. When combined with exercise, AAS have been found to induce mild hypertrophy of the cardiac myocytes and impair the cardiac microvascular adaptation to physical conditioning [32,33]. Based on these findings, we hypothesize that alterations of the heart structure in human subjects due to AAS administration are very likely to occur, but that they can not be detected by current echocardiographic examination methods since such heart damage primarily seems to occur at the cellular level. Previously, Melchert and Welder provided already the theoretical base for our conclusion [17]. Consequently, routine cardiological examinations may provide incomplete assessment of the cardiac condition in AAS using athletes leading to undeserved reassurance.

Conclusions

From this study we conclude that the short-term administration of AAS does not lead to detectable echocardiographic alterations of heart morphology, systolic and diastolic function in experienced strength athletes. This applies for the administration of a high therapeutic dose (200 mg per week, i. m.) of a single anabolic steroid (nandrolone decanoate) for eight weeks, as well as for AAS polydrug regimens in suprapharmacological doses during periods up to 16 weeks. Since the detrimental effects of short-term AAS administration on the heart are well described in animal studies using (ultra-)microscopic evaluation of heart cell structures, the results of the present study must be interpreted with caution. Therefore, echocardiographic evaluation may provide incomplete assessment of the actual cardiac condition in AAS users since it is not sensitive enough to detect alterations at the cellular level. From the present study no conclusions can be drawn of the cardiotoxic effects of long term AAS abuse.

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