Original Article

Evaluation of the Effects of Anabolic Steroids on Right and Left Ventricular Functions in Bodybuilders

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ABSTRACT

Background: Anabolic-androgenic steroids (AASs) misuse for improving exercise ability and muscle mass in bodybuilders is ever-increasing and it is suggested to be responsible for destructive cardiovascular effects. In this study, we sought to assess all structural and functional aspects of left ventricular (LV) and right ventricular (RV) functions in male bodybuilding athletes who consume long-term AASs.

Methods: The present study was conducted in Kerman in 2016. Based on a cross-sectional study, 52 bodybuilders were selected and divided into 2 groups (26 cases in each group). As a control group, 20 healthy sedentary volunteers with the same age and body mass index (BMI) as the previous 2 groups were selected.

Results: Except for LV end-systolic diameter, LV end-systolic volume, and A/E in the Doppler assessment, there were significant differences between all the parameters of LV structure and function, consisting of LV end-diastolic diameter, interventricular septal diameter, LV posterior wall diameter, LV end-diastolic volume, LV mass, LV mass index, deceleration time in mitral inflow Doppler evaluation, and tissue Doppler imaging (TDI) parameters between AAS users, nonusers, and control groups (all *P*s<0.05). Additionally, RV size, fractional area change, tricuspid annular plane systolic excursion, and TDI evaluation of the lateral point of the tricuspid annulus as parameters of RV function were significantly different between the mentioned groups (all *P*s<0.05).

Conclusions: Our study showed that multiple courses of AAS abuse by young male bodybuilders could lead to detrimental effects on LV and RV morphology and systolic and diastolic functions over time. Therefore, it is essential to raise awareness among young athletes regarding the chronic side effects of these compounds. ***(Iranian Heart Journal 2022; 23(4): 38-45)***

KEYWORDS: Stanozolol, Left ventricle, Right ventricle, Transthoracic echocardiography

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Received: February 2, 2021 **Accepted:** April 17, 2022

Anabolic-androgenic steroids (AAS) constitute a familiar name for synthetic substances related to the male sex hormones (eg, testosterone). They promote the growth of skeletal muscles (anabolic effects) and the development of male sexual characteristics (androgenic effects) in both males and females. AASs were developed in the late 1930s primarily to treat hypogonadism, a condition in which the testes do not produce sufficient testosterone for normal growth, development, and sexual functioning. The primary medical uses of these compounds are to treat delayed puberty, some types of impotence, breast cancer, and wasting of the body due to muscular atrophy and anemia caused by HIV infection or other chronic diseases.[1]

AAS abuse differs from the abuse of other illicit substances because the initial abuse of anabolic steroids is not driven by the immediate euphoria that accompanies most drugs of abuse such as cocaine, heroin, and marijuana, but by the desire of abusers to change their appearance and performance, characteristics of great importance to adolescents. The effects of steroids can boost confidence and strength, leading abusers to overlook the potentially serious and long-term damage that these substances can cause.[3]

Today, unfortunately, one of the most common reasons for the consumption of these compounds is to decrease fat tissue, increase muscular mass, and improve exercise capacity in young bodybuilders. Doses taken by abusers can be 10 to 100 times higher than those used for medical conditions.[2] The most important side effects of these compounds are salt and water retention, elevated blood pressure, increased LDL and total cholesterol, decreased HDL, acne and hair loss, decreased libido, azoospermia, testis atrophy, gynecomastia, menses disorder in women, psychological disorders such as excitability and aggressive behavior, a wide range of liver problems (elevated liver enzyme and jaundice to hepatocellular carcinoma), and musculoskeletal effects leading to short stature.[4-8]

The cardiovascular side effects of chronic abuse of AASs are endothelial dysfunction, increased peripheral vascular resistance, premature atherosclerosis, prothrombotic conditions, morphological and functional abnormalities such as myocardial hypertrophy, dilation of the heart chambers, abnormality of diastolic function and relaxation properties, and subclinical systolic impairment.[9-11] In recent years, different modalities such as the exercise test, echocardiography, and cardiac magnetic resonance imaging have been used to evaluate cardiac morphologic and functional abnormalities due to AAS abuse. The echocardiographic parameters mostly applied for the assessment of morphological and functional changes in different studies are left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), interventricular septal thickness (IVSD), LV posterior wall thickness (LVPWDD) by the M-mode method, and the evaluation of diastolic function by the Doppler method, strain rate imaging, and tissue Doppler imaging.[12,13]

Although different studies have evaluated the structural and hemodynamic effects of AAS chronic use on the LV, the results are controversial, and more importantly, the effects of these compounds on right ventricular (RV) structure and function are a novel issue that has yet to be assessed. In this study, we endeavored to evaluate all the structural and functional aspects of the LV. Furthermore, we sought to be among the first investigators to assess the effects of AAS abuse on RV size and function. Significant differences and notable controversies between the previous studies, the unknown effects of AAS abuse on RV structure and function, and

more significantly, the involvement of one of the most important parts of society, young athletes, with this complex issue, motivated us to start this project.

METHODS

In the present cross-sectional study in Kerman, in southeast Iran, more than 200 young bodybuilders were selected between August 2016 and November 2012 from more than 10 bodybuilding clubs and powerlifting training centers. According to a previous study,[19] the sample volume was calculated to be 20 persons in each of the 2 groups. To augment the accuracy of the study, we added 20% to each group, so that the sample volume reached 26 persons in each group. The method of the calculation of the sample volume was as follows:

The estimated sample size for a 2-sample comparison of means:

Test Ho: m1 = m2, where m1 is the mean in population 1 and m2 is the mean in population 2 Assumptions:

alpha = 0 . 0 5 0 0 (2-sided)

Power = 0 . 9 0 0 0

m1 = 202

m2 = 249

sd1 = 52

sd2 = 33

n2/n1 = 1.00

Estimated required sample sizes n1 = 20

n2 =20

After initial interviews and personal history taking, 52 bodybuilders with a daily practice of a minimum of 2 hours and at least 3 times per week for the preceding 2 years were selected and divided into 2 groups (26 cases in each group): Group I with chronic AAS abuse for at least 16 weeks of testosterone or nandrolone injection and Group II, which included athletes without a history of anabolic AAS abuse. The source of personal history to determine exercise duration and whether the subjects abused AASs were recorded from the athletes themselves and their coach, and a checklist was used to record the information. For ethical reasons, prohibition of AAS use, and better cooperation and acceptable reliability of the athletes, they were reassured that their data would be confidential and would not be published anywhere except for research purposes. As a control group, 20 healthy sedentary volunteers with the same age and body mass index (BMI) as the previous 2 groups were selected.

First, by taking an exact medical history, performing general examinations, cardiovascular physical examinations, and 12-lead electrocardiography at rest, athletes with any evidence of cardiovascular disease were identified and excluded from the study. The exclusion criteria were composed of a history of hypertension, valvular stenosis, and preexisting bundle branch blocks in electrocardiography.

Two-dimensional and color Doppler echocardiography and tissue Doppler imaging (TDI) were performed for all the subjects thereafter. Two-dimensional and M- mode echocardiographic examinations were carried out to determine LVESD, LVEDD, and (LVPWDD in the diastole. The LV global ejection fraction (EF) was estimated as well. Additionally, LVESV and LVEDV were measured by the Simpson method. LV mass was calculated via the following formula:

LV mass=0.8{1.04[(LVEDD+IVSd+Pwd) ^3-LVEDD^3]} +0.6

Subsequently, the LV mass index was calculated through the division of LV mass by body surface area (BSA).

For BSA measurement, the DuBois formula (BSA=0.007184×height^0.725×weight^0.425) was used.

Diastolic function was evaluated by Doppler echocardiography based on the peak transmitral flow velocities during early diastolic filling (E), atrial contraction (A), E-to-A ratio, and E-wave deceleration time, measured at the tips of the mitral valve leaflets in the apical 4-chamber view. For TDI assessment, peak myocardial velocities were measured during the systole as well as early and late diastolic filling at the medial mitral valve annulus, the base of the septal wall, and the base of the lateral wall points. The specific and novel characteristic of this study as mentioned earlier was the evaluation of RV systolic and diastolic functions, as well as the estimation of pulmonary artery systolic pressure. After the measurement of basal and mid-cavitary diameters, RV systolic function was estimated via the fractional area change (FAC) by the Simpson method. In addition, tricuspid annular plane systolic excursion (TAPSE) was measured by the M-mode, and diastolic function was assessed by the TDI method performed by the assessment of peak RV myocardial velocities measured in the same way as the LV at the lateral tricuspid annulus point. Pulmonary arterial pressure was estimated using the tricuspid flow gradient. One-way ANOVA was used to compare the groups. Statistical analyses were performed using Stata software, version 12.0 (Stata Corp, College Station, TX, USA)

RESULTS

Table 1 presents the demographic characteristics of the cases in each group. As is demonstrated by the table, no significant differences existed between the 3 groups.

Table 2 illustrates LV chamber diameters, volumes, mass, and mass index, as well as Doppler findings.

Except for LVESD and LVESV, there were significant differences in the other parameters of LV structure between all the 3 groups. LVEDD (P=0.008), IVSD (P<0.001), LVPWDD (P<0.001), and LVEDV (P=0.003) were significantly larger in Group I (AAS users) than in the other 2 groups. Further, LV mass (P<0.001) and LV mass index (P<0.001) were significantly larger in Group I than in the other 2 groups.

Diastolic function based on E/ A ratio was not significantly different between the 3 groups. Nonetheless, in TDI evaluation (Table 3), early and late diastolic filling and systolic contraction peak myocardial velocities were significantly lower in Group I than in the other 2 groups.

As is presented in Table 4, in the evaluation of RV size, there were significant differences in basal and mid-cavitary RV diastolic diameters between the 3 groups. Moreover, in the assessment of RV function, FAC (P=0.014) and TAPSE (P=0.039) were significantly lower in Group I than in the other 2 groups. In TDI assessment, except for systolic contraction peak myocardial velocity, the other TDI parameters at the lateral point of the tricuspid annulus were significantly lower in Group I than in the other 2 groups.

Table 1: Demographic characteristics of the study population

Variables	Users* **Mean (SD)**	nonusers **Mean (SD)**	Controls **Mean (SD)**	*P* value
N	26	26	19	
Age	24.28(3.63)	25.43(4.52)	26.11(5.21)	0.065
Body mass index	26.32(1.45)	25.61(2.88)	24.78(2.54)	0.42
Exercise	4.66(1.32)	5.11(1.66)	-	0.12

Table 2: Results of standard and transmitral Doppler echocardiography

Variables	Users **Mean (SD)**	nonusers **Mean (SD)**	Controls **Mean (SD)**	*P* value
LVEDD	54.12(6.19)	49.77(5.94)	49.26(4.78)	0.008
LVESD	34.24(38.99)	32.56(36.36)	32.86(37.45)	0.320
LVEDV	101.27(26.25)	85.19 (13.42)	95.63(11.49)	0.003
LVESV	46.15(15.52)	39.53(9.22)	42.68(6.41)	0.121
LVPWD	11.33(1.95)	10.73(1.61)	9.00(1.66)	0.00
IVSD	11.62(1.62)	10.10 (1.68)	9.05(1.64)	0.00
LVEF	53.73(5.39)	57.62(3.62)	57.89(4.90)	0.004
E/A	1.36(.43)	1.37(.30)	1.31(.14)	0.825
LV mass	257.99	194.99 (54.35)	153.74 (22.04)	0.00
LV mass index	123.61	96.05 (26.56)	77.42 (10.89)	0.00

Table 3: Results of tissue Doppler imaging at the mitral valve annulus, the base of the septal wall, and the base of the lateral wall

Variables	Users Mean (SD)	nonusers Mean (SD)	Controls Mean (SD)	*P* value
MVS	7.53(1.33)	8.42(1.92)	8.83(.91)	0.014
MVE	9.73 (2.18)	11.34(1.99)	11.86 (1.41)	0.007
MVA	7.53(1.88)	8.42 (2.12)	9.73 (1.14)	0.002
SWS	7.42 (1.65)	8.26 (2.25)	9.06 (1.17)	0.013
SWE	9.69 (1.87)	11.40 (2.00)	11.82 (1.48)	0.00
SWA	6.68(1.21)	8.19(2.38)	10.13 (1.34)	0.00
LWS	9.16 (2.63)	10.96 (2.93)	10.99 (.98)	0.036
LWE	12.46 (2.84)	13.59 (2.48)	13.22 (1.05)	0.006
LWA	8.44 (2.96)	8.98 (2.24)	11.98 (1.64)	0.00

Table 4: Results of the evaluation of RV systolic function, TDI at the lateral tricuspid annulus, and PASP estimated via TRG

Variables	Users Mean (SD)	non users Mean (SD)	Controls Mean (SD)	*P* value
RV basal diameter	39.50(2.47)	37.84(2.94)	35.47(2.11)	<0.001
RV	34.03(2.56)	32.96(2.64)	30.78(2.91)	<0.001
FAC	0.37(0.07)	0.43(0.07)	0.40(0.03)	0.014
TAPS	1.98(0.46)	2.25(0.32)	2.17(0.33)	0.039
LTVS	11.15 (2.30)	12.26 (1.80)	12.13 (0.96)	0.122
LTVE	12.65 (3.21)	14.76 (2.67)	14.27 (0.95)	0.003
LTVA	10.42 (3.21)	11.03 (2.48)	12.86 (2.05)	0.004
TRG	23.35 (7.42)	17.46 (3.27)	20.79 (3.56)	0.001
PAP	29.81 (7.93)	23.27 (3.72)	22.63 (4.66)	0.001

DISCUSSION

Our findings showed a significant difference in echocardiographic parameters between the AAS group and the other 2 groups, except for LVESD, LVESV, and E/A in the Doppler assessment of mitral inflow and systolic contraction peak RV myocardial velocity at the lateral point of the tricuspid annulus.

We also found that AAS-using bodybuilders in Group I showed eccentric LV hypertrophy with larger cavity size and thicker ventricular septal and posterior wall (larger LV mass and LV mass index) in contrast to bodybuilders in Group II who did not use AASs. Eccentric LV hypertrophy, observed in this study, is in disagreement with the results of a study conducted in 2009, demonstrating concentric

hypertrophy as a result of chronic AAS abuse.[14] There is a very important indicator for the exact evaluation of the nature of ventricular hypertrophy named "relative wall thickness (RWT)", which is calculated by the following equation:

RWT=2PW/LVEDD.

The cutoff value for RWT is 0.42. If RWT is greater than 0.42, it means that concentric hypertrophy has occurred, and if it is below 0.42, it denotes eccentric hypertrophy.[15] In our study, RWT in the user and nonuser groups was 0.403 and 0.44, respectively, which suggested concentric hypertrophy in the nonuser group and eccentric hypertrophy in the user group. These differences could be related to multiple and unlimited courses of AAS abuse by young bodybuilders without any supervision from their coaches or educators, leading to LV systolic dysfunction and significantly reduced EF. AAS dosage applied in the majority of studies was 200 to 250 mg of testosterone weekly, in contrast to 750 mg per week of testosterone consumed by the athletes in our study. In 2010, Baggish et al[16] reported that high doses of AASs could lead to significant LV dysfunction and reduced EF dramatically. The AAS dosage consumed in the mentioned study was 675 mg per week in contrast to the usual dosage of 250 mg per week in the others. In their study, the average EF in the control group and the AAS group was 59% and 51%, respectively, and half of the athletes had EF below 50%. This important finding shows a statistically significant relationship between the AAS dosage and the severity of drug effects. Our results, chiming in with the findings of the Baggish study, are suggestive of a causative relationship between the consumption of a high dose of AASs and the occurrence of eccentric LV hypertrophy, significant LV dysfunction, and reduced EF. In a previous investigation, mentioned above, in the assessment of diastolic function by Doppler, there were significant differences in TDI parameters.[14] Hence, the results of that study support our findings in TDI evaluation.

In a study published in 2012, the only significant difference was in LV septal and free wall thickness between the AAS group and the control group. In addition, no significant difference was found between the user and nonuser groups.[17] In contrast, in our study, as was cited above, we found significant differences between all 3 the groups in the majority of parameters.

Andrea et al[18] in 2007 reported significant differences in LVEDD and LVEF, which supports our findings. In a study published in 2010 by Montisci et al,[19] LV mass and LV mass index were significantly larger in the ASA group than in the other groups; nevertheless, an assessment of systolic function yielded no significant differences between the 3 groups. In tissue Doppler imaging, the peak myocardial velocity in the AAS group was significantly lower than that in the other groups. In this study, the method of TDI has been introduced as an effective and reliable modality for the early diagnosis of diastolic function disturbances. Krieg et al[15] in 2007 reported significant differences in LV septal thickness, LV mass index, and TDI parameters and nonsignificant differences in A/E between AAS-using bodybuilders and 2 other groups. Accordingly, their results are in agreement with our findings. As was mentioned earlier, in the present study, we took the initiative of evaluating AAS effects on the structure and function of the RV. In the evaluation of the RV structure by basal and mid-cavitary diastolic diameters and the assessment of RV function by FAC, TAPSE, and TDI evaluation, in conjunction with the estimation of pulmonary artery systolic pressure, except for S' at the lateral point of the tricuspid annulus, there were significant differences in parameters between the AAS group and the other 2 groups.

CONCLUSIONS

Our study showed that multiple courses of AASs by young male bodybuilders could lead to detrimental effects on cardiac morphology and function, including LV dilation, wall thickening, reduced EF, impaired relaxation, LV diastolic dysfunction, RV enlargement, RV systolic and diastolic dysfunction, and pulmonary artery hypertension. Consequently, we suggest that awareness should be raised among young athletes concerning the destructive side effects of the chronic misuse of such compounds as a pivotal component of primary prevention in sports.

REFERENCES

1. What are Anabolic stroids? web medical reference from Healthwise, April201
2. Christion nordquist, what is Anabolic stroid? MNT.Know ledge center ,june 2012
3. Nova D.Volkow, M.D., Anabolic stroid abuse, National institute on Drug abuse, Augest 2006
4. HartgensF, Kuipers H: Effects of androgenic anabolic steroids in athletes,outpatient Sportsmodicine and sports medicine center muastricht, 2004; 34(8):513-514
5. Evans NA: current concepts in anabolic androgenic steroids, the amorican journal of sports medicine, 2004 march 32(2): 534-42
6. Achar S, Rostamian A , Narayan SM :cardiac and metabolic offects of anabolic – androgenic steroid abuse on lipid and blood pressure , American journal of cordiology 2010 sep, 15; 106(6):893-901
7. Melnic B, Jansen T, Grabbe S: abuse of anabolic androgenic steroids and bodybulding acne, Journal der deutschen Gesellschaft, 2007 feb; 5(2):110-7
8. Di luigi, Romonelli F, lenozi A: Androgenic anabolic steroid abuse in male , journal of endocrinological investigation 2005; 28(3suppl) :81-4
9. Kinderman W:cardiovascular side effects of anabolic androgenic stroids,kardiovaskulare kardiovaskular nebenwir kungen von anabol-androigenen stroiden, 2006 sep; 31(6):566-73
10. Vanberg P, Atar D: androgonic anabolic steroid abuse and cardiovascular system, handbook of experimental pharmacology 2010; (195):411-57
11. melchart RB, welder AA: cardiovascular effects of androgenic anabolic steroids, medicine and science in sports and exercise, 1995 sep; 27(9):1252-62
12. hajimoradi B, Kazerani H: Echocardiographic findings in power athletes abusing anabolic androgenic steroids, Asian journal of sports medicine, 2013 march; 4(1):10-4
13. arhausen A, Albers T, Kinderman W: Are the cardia effects of anabolic steroid abuse in strength athletes reversible? (British cardiac society), 2004 may, 90(5); 496-501
14. Ilic I, Dgordjevic v, stankovic I, Vahovic – stipac A, et al: the impact of anabolic and androgenic steroids abuse and type of training on left ventricular remodeling and function in competitive athletes, mortality – medical and pharmaceutical review 2014 Apr; 71(4):383-9
15. Krieg A, scharhag J, Albeost. Kinderman W, uohausen A: cardiac tissue Doppler in steroid users. International journal of sport medicine 2007 AUG, 28(8):638-43
16. Andrea A, caso p, salerno G, scalafile R, De corato g, et al: Left ventricular early myocardial dysfunction after chronic misuse of anabolic androgenic steroids :a Doppler Miocardial and strain imaging analysis, British journal of sports medicine 2007 may; 41(3):149-55
17. Montisci M, El Mazloum R, Cecchetto G, Terranova C, Ferrara SD, Thiene G, et al. Anabolic androgenic steroids abuse and cardiac death in athletes: morphological and toxicological findings in four fatal cases. Forensic science international. 2012; 217(1-3):e13-e8.

18. Wu ET, Akagi T, Taniguchi M, Maruo T, Sakuragi S, Otsuki S, et al. Differences in right and left ventricular remodeling after transcatheter closure of atrial septal defect among adults. Catheterization and Cardiovascular Interventions. 2007; 69(6):866-71.

19. Montisci R, Cecchetto G, Ruscazio M, Snenghi R, Portale A, Viel G, et al. Early myocardial dysfunction after chronic use of anabolic androgenic steroids: combined pulsed-wave tissue Doppler imaging and ultrasonic integrated backscatter cyclic variations analysis. Journal of the American Society of Echocardiography. 2010; 23(5):516-22.