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Anabolic Steroids Use Is Associated with Impairments in Atrial and Ventricular Cardiac Structure and Performance in Athletes

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Purpose:

Despite potential severe cardiac side effects, anabolic androgenic steroids (AAS) are increasingly used by strength athletes. However, previous echocardiographic studies focused on the left ventricular (LV) strains but did not assess LV twist and untwist mechanics. Moreover, left atrial (LA) function has been often neglected, and its stiffness, an important determinant of LA reservoir function, has never been challenged. The aim of this study was to investigate the effects of AAS on LA and LV morphologies and functions in strength athletes.

Methods:

Fifty subjects including 20 strength-trained young athletes age 32.0 ± 8.5 yr with a mean duration of AAS use of 4.7 ± 1.8 yr (users), 15 athletes with no history of AAS use (nonusers) and 15 sedentary controls underwent speckle tracking echocardiography to assess LA and LV morphology and function. Results: Users showed higher LA reservoir dysfunction than nonusers ($33.7\% \pm 10.9\%$ vs $44.9\% \pm 9.9\%$ respectively, $P = 0.004$) and higher LA stiffness (0.13 ± 0.05 vs 0.19 ± 0.08 A.U., respectively; $P = 0.02$), higher LV mass index and lower global and regional LV diastolic and systolic dysfunction (global longitudinal strain: $-15.5\% \pm 3.2\%$ vs $-18.9\% \pm 1.8\%$ respectively; $P = 0.003$), with a drop of LV twist–untwist mechanics (untwisting velocity: $61.5^\circ\text{s}^{-1} \pm 20.2^\circ\text{s}^{-1}$ vs $73.7^\circ\text{s}^{-1} \pm 16.1^\circ\text{s}^{-1}$ respectively, $P = 0.04$). There were significant correlations between LV mass and LV apical rotation ($P = 0.003$, $r = 0.44$) and diastolic longitudinal strain rate ($P = 0.015$, $r = 0.33$).

Conclusions:

Our results showing significant LA and LV remodeling and dysfunctions in young AAS using athletes are alarming. Screening echocardiography based on speckle tracking echocardiography parameters for early diagnosis, as well as a stronger awareness in athletes and in physicians are warranted in this context.

Anabolic androgenic steroids (AAS) are increasingly used to improve muscle mass and strength. The misuse of these drugs can lead to major cardiovascular events and sudden cardiac death (1). Anabolic androgenic steroids are frequently used not only in elite competitive bodybuilders, but also in young recreational strength-trained athletes (2). Previous cardiac imaging studies have documented preclinical evidence of AAS cardiotoxicity in forms of left ventricular (LV) hypertrophy (3), myocardial dysfunction (3,4), fibrosis (1,4), increased coronary artery calcification, and plaque volume (4).

In line with autopsy reports (1), most echocardiographic studies reported LV hypertrophy in AAS users (4,5), whereas others showed no significant increase in LV mass (LVM) (6,7). As some (5,8) but not all studies included both nontraining control and strength-trained AAS nonusers groups, it was difficult to differentiate the effects due to AAS use or to strength sport

itself (4,6,9). Although initial studies, limited to standard echocardiographic parameters, found no evidence for systolic and diastolic dysfunction (10), more recent reports based on tissue Doppler imaging (TDI) or speckle tracking echocardiography (STE) detected early LV dysfunction in AAS using athletes (4,11). Baggish et al. (4) recently demonstrated that systolic dysfunction in AAS consuming athletes recovered after discontinuation, whereas diastolic dysfunction appeared less reversible. Left ventricular twist–untwist mechanics, which have been shown to be impaired in different forms of LV hypertrophy (12,13) have not yet been analyzed in this context. Left ventricular twist improves ejection fraction (EF) and energy stored in elastic components. This energy is restored very early in diastole, creating an intraventricular pressure gradient that favors LV filling, thus linking systole to diastole (e.g., systolic–diastolic coupling) (14). In line with their depressed diastolic function (3,4), LV twisting and untwisting could be blunted in strength trained athletes using AAS, but it remains to be confirmed. Left atrial (LA) morphology and function have also been neglected in previous studies. The LA is a complex and active chamber, which acts as a reservoir during ventricular systole and favors ventricular filling during diastole by its role as a conduit and booster pump. Recent investigations have suggested that LA parameters might be clinically useful for risk stratifications, being related to adverse cardiac events, such as atrial fibrillation, heart failure and mortality in patients with LV diastolic dysfunction (15). Moreover, LA stiffness, an important determinant of LA reservoir function, was increased in pathological states including LV hypertrophy (16,17) To our knowledge, only D’Andrea et al. (11) documented LA enlargement and dysfunction in AAS using athletes, but they did not assess LA stiffness that could be increased in this specific population.

In this context, we aimed to evaluate LV and LA morphologies and functions by STE in two groups of young strength-trained athletes (AAS users vs nonusers), compared with age-matched controls. We hypothesized that AAS use would lead to 1) LV and LA remodeling, 2) LV systolic and diastolic dysfunction including impaired twist–untwist mechanics, 3) LA stiffness and dysfunction.

METHODS

Study Population

Twenty strength-trained athletes actively taking AAS for >2 yr (users), 15 strength-trained athletes who had never taken AAS (nonusers) and 15 age-matched healthy sedentary controls (controls) were prospectively included. Because many female bodybuilders have mammary prostheses, which do not allow for good echocardiographic imaging quality, only male subjects were included. All subjects were age 18 to 40 yr. Strength-trained subjects were recruited by advertising in French gymnasiums and had a training history of minimum 5 yr with at least 7 h of training per week. Users were known to participate in bodybuilding competitions and had a documented self-reported history of AAS use for at least three courses of 2 wk in the last 2 yr. All were on-drugs, that is, with their last AAS administration during the last 2 d. Nonusers were known to participate in regional or national competitions of athletic strength and had a self-reported history of never taking AAS. None of the sedentary and strength-trained subjects practiced more than 2 h aerobic sports per week.

Exclusion criteria were coronary artery disease, congestive heart failure, valvular heart disease, treatment for hypertension, respiratory or metabolic disorders, or active cigarette smoking. All subjects were in sinus rhythm. Written informed consent was obtained from

each subject and the study was approved by the French ethical committee in sports science (CERSTAPS no 2018-04-10-28).

Medical Interview and Examination

All participants were systematically asked about doping or performance enhancing drugs in a confidential manner. The type of the drug, dosage, method of administration, number of courses and durations were assessed. All subjects were then examined for body mass and blood pressure.

Echocardiographic Recordings

Echocardiography was carried out with the subject in left lateral decubitus position, with the Vivid Q system (GE Healthcare, Horten, Norway) using a 3.5-MHz transducer. Cine loops were recorded in parasternal short axis, parasternal long axis, and apical views and saved for blinded offline analysis (EchoPAC, BT113; G.E. Healthcare). Grayscale images were saved at a frame rate of 80 to 90 frames per second and color tissue velocity images at a frame rate of 120 to 140 frames per second. All measurements were averaged from five cardiac cycles. Speckle tracking echocardiography was performed in accordance with guidelines of American Society of Echocardiography and European Association of Cardiovascular Imaging (18).

Echocardiographic Analysis

LV morphology and function.

The LV diameters and myocardial thickness were measured from the parasternal long axis view. The LVM was estimated using recommendations (18) and indexed to body surface area (LVMI). Left ventricular diastolic function was assessed from peak early (E wave) and atrial (A wave) transmitral flow velocities. Tissue Doppler imaging velocities (peak E', A', and S') were assessed at the mitral annular level in the different apical 4-chamber view (A4C). Peak E' average from septum and lateral walls (on A4C) and E/E' ratio was used as indices of LV relaxation and LV filling pressures, respectively (19). Left ventricular systolic function was assessed by EF based on the Simpson's biplane method, and by stroke volume and cardiac output evaluated from the apical five chamber and parasternal long axis views for left ventricular outflow tract diameter assessment.

LV strain and twist mechanics.

Systolic global longitudinal strain (GLS) and circumferential strains, diastolic longitudinal and circumferential strain rates (LSr and CSr) and twist mechanics (apical rotation, basal rotation, peak twist, and untwisting rate) were obtained as previously detailed (20). Data were normalized to percentage of systolic duration to avoid differences in heart rate and frame rates. Left ventricular twist was calculated as the difference between apical and basal rotations at each percentage of systolic duration. We considered GLS, circumferential strains, LV rotations and peak twist as indices of myocardial systolic function, LSr and CSr as indices of LV relaxation (21) and peak untwisting rate as an index of LV diastolic suction.

TABLE 1. Androgenic anabolic steroids consumption reported by athletes of the users group.

	No. Users (of 20)	Form	Mean Dosages (mg·wk ⁻¹)	Range of Dosages (mg·wk ⁻¹)	Mean Protocol Duration (wk)	Mean History (yr)
Testosterone	17	Intramuscular	607 ± 247	400-1000	19 ± 4	9.0 ± 2.5
Nandrolone	14	Intramuscular	475 ± 150	350-600	11 ± 2	5.0 ± 1.0
Decabolone	14	Intramuscular	350 ± 75	250-500	12 ± 2	5.0 ± 1.5
Trenbolone	10	Intramuscular	450 ± 25	400-500	10 ± 2	7.0 ± 1.5
Masterone	5	Intramuscular	450 ± 50	300-500	10 ± 3	5.0 ± 1.0
Boldenone	3	Intramuscular	450 ± 50	300-500	12 ± 3	6.0 ± 1.5

LA morphology and function.

LA morphology was assessed by measuring the LA volume index (LAVI) using the biplane area-length method at the A4C and 2-chamber views (18). Deformation analysis of the LA was performed by STE in apical four-chamber views according to the methodological recommendations of Vieira et al. (22). Left atrial endocardial border was manually traces, starting from the septal aspect of the mitral valve annulus. The minimal width of the region of interest was selected. Left atrial longitudinal strain curves were used to assess LA reservoir function during LV systole (first peak), LA booster pump function during active LA contraction (second peak) and LA conduit function during early passive LV filling (difference between first and second peak). Left atrial stiffness index calculated as E/E' to peak LA strain ratio (23).

Statistical Analysis

Analysis was performed using Statview 5.5 (SAS). All values were expressed as mean ± SD, excepted for box plots which were made using median and quartile. For each group, the normality of the distribution was checked by the Kurtosis and Skewness coefficient. One-way ANOVA was used to compare groups and Tukey post hoc test when appropriate. Correlations were determined between LVM and parameters of LV function using Pearson single linear regression test.

RESULTS

Clinical data of the study populations.

Details of AAS consumption reported in the users are presented in Table 1. Users were taking 3.5 ± 1.0 AAS simultaneously, including testosterone, nandrolone decanoate, decabolone, trenbolone, masterone, and boldenone. The mean AAS dosage was 538 ± 228 mg·wk⁻¹, mainly administered by intramuscular injections. All subjects were on-drugs, that is, their last AAS injection was done in the last 48 h before the resting echocardiography. Clinical data are presented in Table 2. Body mass, body surface area, and systolic blood pressures were higher in strength-trained groups compared with Controls.

TABLE 2. Clinical data and left ventricular morphology of the study populations.

	Controls (n = 15)	Nonusers (n = 15)	Users (n = 20)
Clinical data			
Age (yr)	31.1 ± 8.2	27.2 ± 4.5	30.8 ± 7.1
Body height (cm)	175.8 ± 5.7	178.6 ± 6.2	179.8 ± 7.5
Body mass (kg)	71.7 ± 8.7	87.4 ± 11.1*	91.8 ± 9.6*
Body surface area (m ²)	1.86 ± 0.11	2.05 ± 0.14**	2.1 ± 0.14*
Systolic blood pressure (mm Hg)	114 ± 7	130 ± 11*	125 ± 8**
Diastolic blood pressure (mm Hg)	74 ± 6	71 ± 8	76 ± 7
Heart rate (bpm)	62 ± 9	67 ± 14	68 ± 10
Training volume (h·wk ⁻¹)	0.6 ± 0.3	8.9 ± 1.7*	8.8 ± 0.4*
Training experience (yr)	—	10.6 ± 2.3	11.8 ± 0.4
Left ventricular morphology			
LV septum thickness (cm)	0.94 ± 0.10	1.10 ± 0.20***	1.29 ± 0.23******
LV posterior wall thickness (cm)	0.75 ± 0.11	1.05 ± 0.18*	1.15 ± 0.17*
LV end-diastolic diameter (cm)	5.1 ± 0.3	5.5 ± 0.3**	5.7 ± 0.5*
LV end-systolic diameter (cm)	3.2 ± 0.2	3.5 ± 0.2**	3.7 ± 0.4******
LV end-diastolic volume (mL)	96 ± 16	123 ± 17**	143 ± 29*****
LV end-systolic volume (mL)	37 ± 8	45 ± 8***	58 ± 14******
LV mass (g)	155 ± 30	237 ± 46*	297 ± 69******
LV mass index (g·m ⁻²)	83 ± 17	116 ± 18*	141 ± 29******
Relative wall thickness	0.33 ± 0.04	0.39 ± 0.06***	0.43 ± 0.07******

Values are mean ± SD.

Significantly different from controls (**P* < 0.001).

Significantly different from controls (***P* < 0.01).

Significantly different from controls (***)*P* < 0.05).

Significantly different from nonusers (*****P* < 0.01).

Significantly different from nonusers (******P* < 0.05).

LV morphological parameters.

Left ventricular morphological parameters are presented in Table 2. Left ventricular wall thickness, diameters, mass, and relative wall thickness were higher in both strength-trained groups compared to Controls. Users had significantly higher LVMi due to greater interventricular septum thickness, end-systolic diameter and volume compared with nonusers. According to guidelines of the American Society of Echocardiography and European Association of Cardiovascular Imaging (18), 80% of users (16 of 20) exhibited LV hypertrophy (LVM >115 g·m⁻²) compared with 40% (6 of 15) in nonusers.

LV diastolic and systolic dysfunction.

Parameters of LV function are presented in Table 3. Users showed significantly lower E wave, E/A ratios, TDI E' velocities, as well as LSr and CSr compared with nonusers. E/E' ratios showed no significant difference between groups. Peak untwist rate was lower in users compared with nonusers and controls (Fig. 1A). Kinetics of twisting and untwisting rates during the cardiac cycle (Fig. 1E) showed that peak untwist rate occurs early in all groups with no delay in time to peak in users. Users exhibited lower EF and lower GLS and circumferential strains compared with nonusers. Peak LV twist, resulting from the difference of basal and apical rotation, was significantly lower in users compared with controls (Fig. 1B), due to reduced apical rotations (Fig. 1C), whereas no difference was observed for basal rotations (Fig. 1D). Timing of twisting and rotational events were similar between groups (Figs. 1F, G, and H). Significant correlations were observed between LVM and LSr diastolic (Fig. 2A, *r* = 0.33, *P* = 0.015), as well as apical rotation (Fig. 2B, *r* = 0.44, *P* = 0.003).

TABLE 3. Left ventricular diastolic and systolic function.

	Controls (n= 15)	Nonusers (n= 15)	Users (n= 20)
Standard parameters			
E wave (cm·s ⁻¹)	69 ± 12	79 ± 9*	60 ± 11***
A wave (cm·s ⁻¹)	41 ± 5	44 ± 7	42 ± 6
E/A	1.7 ± 0.3	1.8 ± 0.3	1.5 ± 0.3***
Isovolumetric relaxation time (ms)	81 ± 6	84 ± 7	94 ± 12*****
Stroke volume index (mL·m ⁻²)	39.6 ± 4.1	38.9 ± 5.1	39.3 ± 11.5
Cardiac output index (L·min ⁻¹ ·m ⁻²)	2.4 ± 0.4	2.6 ± 0.5	2.7 ± 0.7
EF (%)	61 ± 4	63 ± 5	58 ± 6***
TDI parameters			
E _{lat} (cm·s ⁻¹)	14.7 ± 2.5	15.8 ± 2.6	12.2 ± 3.1****
A _{lat} (cm·s ⁻¹)	6.7 ± 1.8	7.8 ± 1.3	8.1 ± 1.8*
E _{sept} (cm·s ⁻¹)	12.1 ± 1.9	11.8 ± 2.7	9.3 ± 2.3*****
A _{sept} (cm·s ⁻¹)	7.0 ± 1.1	7.4 ± 1.5	8.4 ± 1.8*
E _{mean} (cm·s ⁻¹)	13.4 ± 1.9	13.9 ± 2.1	10.8 ± 2.5*****
E/E _{mean}	5.2 ± 0.8	5.8 ± 1.1	5.7 ± 1.3
S _{lat} (cm·s ⁻¹)	10.0 ± 1.5	10.6 ± 1.8	9.5 ± 2.5
S _{sept} (cm·s ⁻¹)	8.3 ± 0.9	8.6 ± 1.3	8.0 ± 1.6
STE parameters			
LSr diastolic (s)	1.55 ± 0.3	1.63 ± 0.2	1.20 ± 0.4****
CSr diastolic (s)	2.42 ± 0.45	2.30 ± 0.44	1.7 ± 0.37*****
GLS (%)	-18.5 ± 1.9	-18.9 ± 1.8	-15.5 ± 3.2****
Circumferential strain			
Basal level (%)	20.1 ± 3.1	19.8 ± 3.9	15.6 ± 3.6*****
Apical level (%)	-27.7 ± 4.6	-25.8 ± 4.2	-21.2 ± 3.9*****

Values are mean ± SD.

Significantly different from controls (**P* < 0.05).

Significantly different from nonusers (***P* < 0.001).

Significantly different from nonusers (***)*P* < 0.01).

Significantly different from controls (*****P* < 0.001).

Significantly different from controls (******P* < 0.05).

LSr, longitudinal strain rate; CSr, circumferential strain rate.

LA morphology and function.

Users showed more dilated LA, lower LA reservoir and conduit functions, and a higher LA stiffness index compared with nonusers (Table 4 and Fig. 3). Nonusers showed no signs of morphological or functional changes compared with controls.

DISCUSSION

To our knowledge, this is the first study reporting substantial and consistent changes of LV twist–untwist mechanics and LA morphology, function and stiffness in young AAS using bodybuilders. Compared with nonusers, AAS users showed: (1) LV hypertrophy and LA enlargement, (2) LV diastolic dysfunction including impaired twist–altered untwist mechanics (3) Increased LA stiffness associated with reservoir and conduit dysfunction.

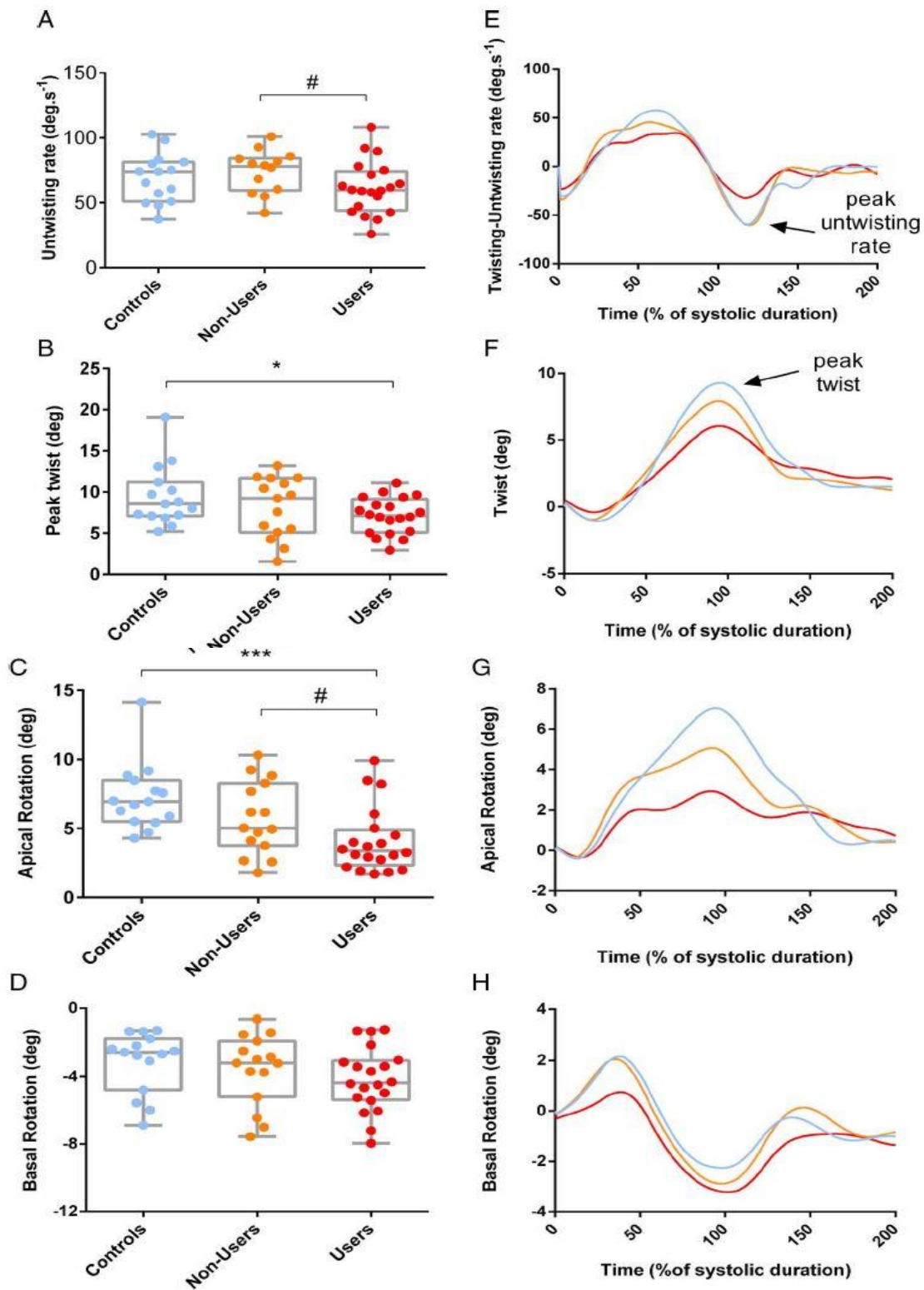


FIGURE 1—Parameters of left ventricular twist–untwist mechanics. On the left, boxplots with individual data shows (A) peak untwisting rate, (B) peak twist, (C) peak apical rotations, (D) peak basal rotations and on the right (E, F, G and H) the timing of twisting-untwisting velocity, twist or peak apical and basal rotations during the cardiac cycle. For each group, data of the curves (E, F, G and H) were averaged at every percent of systolic duration from the data of all subjects (Significantly different from controls (* $P < 0.05$; *** $P < 0.001$); significantly different from nonusers (# $P < 0.05$; ## $P < 0.01$)).

LV hypertrophy and diastolic and systolic dysfunctions.

As expected, when compared with controls, strength trained users and nonusers presented with LV hypertrophy, very likely on account of regular pressure overload related to weight lifting. Furthermore, in users, AAS consumption led to a significantly higher LVMi compared with nonusers, suggesting an anabolic effect not only on skeletal but also on cardiac muscle mass. Of note, 80% of users exhibited an LVMi exceeding the cut-off value of $115 \text{ g}\cdot\text{m}^{-2}$ compared with 40% in nonusers. These data are in line with autopsy reports (1) and other echocardiographic studies reporting massive LV hypertrophy in AAS users (3). However, some (8,11) but not all studies included a nontraining control group (4,6,9), which is mandatory to differentiate effects due to AAS use from those due to strength training itself. Diastolic dysfunction was evidenced by lower early filling (lower mitral E wave and lower E/A ratio) which could be explained not only by impaired relaxation properties (lower TDI E' and lower STE diastolic longitudinal and circumferential strain rates), but also by an altered suction effect of the LV due to a lower peak untwisting rate, while E/E' mean and E/SrL diastolic, both indirect indexes of LV filling pressures, were unchanged in users. Systolic dysfunction was evidenced by lower EF and lower STE deformation indices assessed by GLS, circumferential strains, and LV peak twist. Moreover, parameters of diastolic (LSr) and systolic function (apical rotation) were significantly correlated to LVM (respectively, $r = 0.33$ and $r = 0.44$), suggesting a mechanistic link between LV morphology and functional deterioration. The observed impairment of functional LV indices might be explained by fibrosis and pathological cardiomyocyte growth and activation induced by AAS administration, as suggested by autopsy reports (1) and experimental studies (24). In a recent article, we demonstrated using specific regional LV strain analysis that LV dyssynchrony was higher in users compared with nonusers and controls, that could be an additional mechanism explaining the decrease in their LV function (25).

Our results observed in users “on drugs” during the study period are in line with the large recent study of Baggish et al. (4) who reported diastolic dysfunction assessed by lower TDI early relaxation velocity and systolic dysfunction evidenced by lower EF. Interestingly, systolic dysfunction was reversible in users during their “off-drugs” period, whereas diastolic dysfunction was impaired both in “on-drugs” and “off-drugs” users, suggesting a more permanent form of acquired pathology. However, the diagnosis of diastolic dysfunction was based only on a single echocardiographic criterion in this study.

Left ventricular twist–untwist mechanics, which represent the first main outcome of the present study, have not yet been assessed in AAS users. In our users, the lower LV peak twist resulted from lower apical rotations, while basal rotations were unchanged. This result contrasts with twist mechanics in other forms of pathologic LV hypertrophy. Indeed, patients with hypertrophic cardiomyopathy (26) or with increased afterload due to hypertension (27), show increased LV twist, which has been interpreted as a compensatory mechanism to maintain LV mechanical function. On the contrary, LV hypertrophy in AAS users was associated with a loss of function, analogous to what is observed in patients with heart failure with reduced EF (28) because of ischemic cardiomyopathy (29) or to dilated cardiomyopathy (30). This reduction of LV twist has been linked mechanically to the severe reduction of circumferential strain in the apex (28) to transmural ischemia, local myocardial fibrosis (31). The two latter mechanisms might potentially be involved in AAS use.

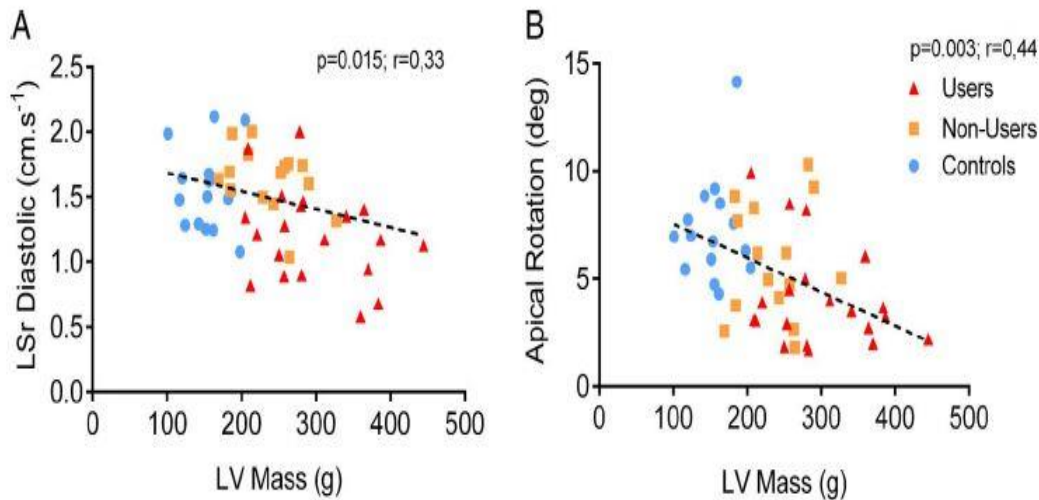


FIGURE 2—Correlation between morphologic and functional parameters in the three study groups. Correlations between left ventricular mass and (A) diastolic longitudinal strain rate (LSr diastolic) and (B) apical rotation. We used Pearson single linear regression test to investigate the correlations.

In our study, the lower peak twist induced lower peak untwisting rates via a systolic–diastolic coupling (32). Lower peak untwisting rates induce lower intraventricular pressure gradients during isovolumic relaxation time with lower suction effect and might thus contribute to lower LV filling (14). Of note, the alterations of twist–untwist mechanics were not found in our nonusers group or in previous studies in athletes (13). Interestingly, Urbano et al. (33) demonstrated that reduced untwisting rate at mitral valve opening is a useful parameter to distinguish between patients with hypertrophic cardiomyopathy and controls. It could, therefore, represent an additional evidence for adverse cardiac remodeling in our AAS users.

LA enlargement and dysfunction in AAS users.

Atrial function is an integral part of cardiac function that has often been neglected. The interplay between LA and LV functions throughout the cardiac cycle (termed LA–LV coupling) has been shown to play a crucial role in many pathophysiological conditions, including different forms of LV hypertrophy (34,35).

Our study showed a significant LA enlargement in users compared with nonusers and controls. Thus, strength training alone had no significant effect on LAVI a result in accordance with previous studies (11,36). Moreover, we observed a significantly higher stiffness index and an impairment in reservoir and conduit function in users. Reservoir dysfunction, which corresponds to the passive stretching of the atrial wall during LV systole, might be explained by higher stiffness index related to atrial fibrosis in AAS users. Other studies in humans showed a high correlation ($r = 0.65$, $P < 0.001$) between lower LA echocardiographic strain and higher stiffness index with the extent of LA fibrosis assessed by electromechanical mapping in patients (37). Furthermore, animal experiments confirmed the association between low LA strain and LA fibrosis evaluated by histological staining (38).

TABLE 4. LA morphology and function.

	Controls (n=15)	Nonusers (n=15)	Users (n=20)
Morphology			
LAVI (mL.m ⁻²)	24 ± 4	24 ± 5	29 ± 6 ^{*,**}
Function			
Reservoir function (%)	40.1 ± 7.9	43.9 ± 10.3	32.1 ± 10.1 ^{***}
Conduit function (%)	26.5 ± 6.5	33.5 ± 10.6	22.3 ± 8.9 ^{***}
Booster pump (%)	12.5 ± 3.9	11.1 ± 3.0	9.7 ± 2.8 [*]
LA Stiffness index	0.13 ± 0.03	0.13 ± 0.05	0.20 ± 0.09 ^{****,*****}

Values are mean ± SD.

Significantly different from controls (^{*}P < 0.001).

Significantly different from nonusers (^{**}P < 0.05).

Significantly different from nonusers (^{***}P < 0.01).

Significantly different from controls (^{****}P < 0.05).

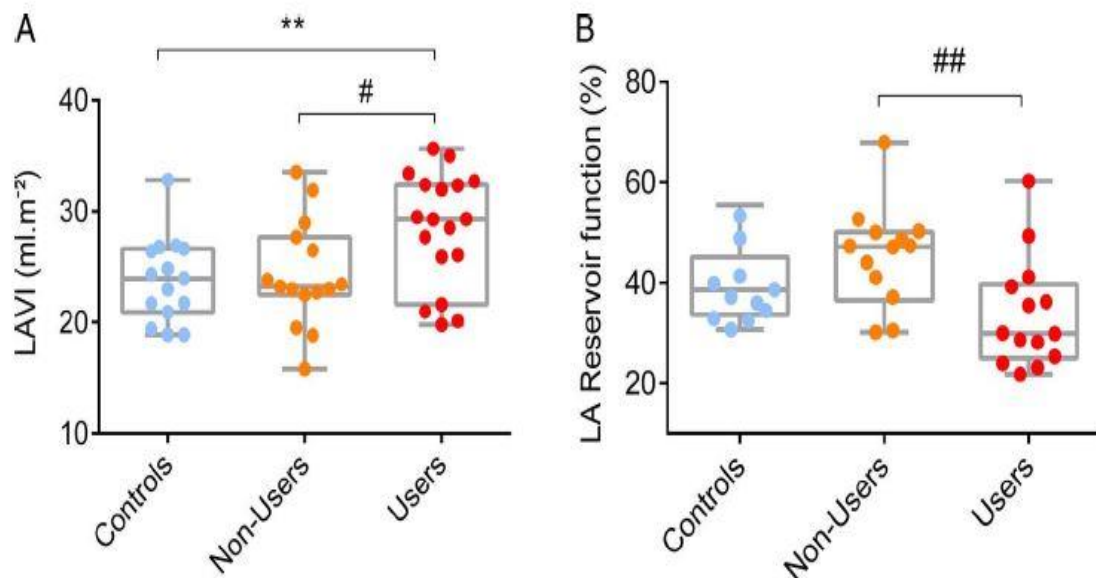


FIGURE 3—Left atrial morphology and reservoir function. Boxplot with individual data shows (A) LAVI, (B) LA reservoir function. ^{***}Significantly different from controls (P < 0.001); Significantly different from nonusers (^{##}P < 0.01; ^{###}P < 0.001).

Only one other study investigated LA morphology and strain in ASS using athletes. D'Andrea et al. (11) showed impaired reservoir and booster pump function. However, these observations were limited to STE lateral wall strain analysis and to 2D emptying fraction, respectively. Interestingly, LAVI ($r = -0.55$, $P < 0.001$), LV E/E' ratio ($r = -0.48$, $P < 0.001$), and the number of weeks of ASS use ($r = -0.51$, $P < 0.001$) were independent determinants of LA lateral strain.

The question arises if LA enlargement, stiffness, and dysfunction are the consequence of the observed LV dysfunction or if these abnormalities are related to direct atrial toxicity of AAS. Indeed, LA function is intimately related to ventricular function throughout the whole cardiac cycle, while also depending on local fibrosis and intrinsic atrial contractility. During LV diastole, the LA is directly exposed to the ventricular pressure through the open mitral valve and the atrial emptying pattern has been shown to be strongly influenced by LV diastolic

properties and filling pressures (15). In the presence of increased LV stiffness, LA pressure rises to maintain LV filling. The increased atrial wall tension leads to chamber dilatation and stretch of the atrial myocardium, triggering myocyte hypertrophy and fibrosis (39).

However, direct atrial toxicity of AAS might also be a plausible mechanism for the observed LA abnormalities. Experimental studies have documented the presence of androgenic receptors in the LA (40). Left atrial walls are significantly thinner than those of the LV and LA function might therefore be affected earlier (41). Experimental data from a heart failure model showed that the atrium is more than 20-fold more prone to fibrosis with faster and larger apoptosis, inflammatory and cell infiltration changes as compared with the ventricle (42). In our study, LV filling pressures, which have been considered to be the main underlying mechanism for LA dysfunction, were not significantly increased in our users. These data are in line with recent findings showing that the degree of LA morphology and function is only modestly related to LV function and LV filling pressures (43) and might be explained by intrinsic atrial pathology. As in other forms of LV hypertrophy (41), LA abnormalities might thus even occur before LV impairment in AAS users and be of particular interest for early detection of cardiac involvement. Both mechanisms, atrioventricular coupling and intrinsic atrial pathology induced by AAS, are likely to overlap and contribute to different degrees in AAS users according to the importance of LV hypertrophy and dysfunction, duration, and cumulated dosage of AAS use or other factors.

Study limitations.

The study population was relatively small, but the bodybuilders were selected based on their high level of practice and on their AAS use, and significant differences were shown for many parameters. Moreover, our users group was compared not only to strength training nonusers but also to nontraining controls to differentiate effects of strength training itself and effects of AAS. Inevitably and for ethical reasons, information about the intake of AAS was self-reported and type of drugs and dosages differed between athletes. Our echocardiographic analysis was focused on LV and LA without evaluation of the right ventricle. Finally, this is a cross-sectional study. Further long-term studies are warranted to determine reversibility and long-term outcome of the observed abnormalities.

CONCLUSIONS

Illicit AAS use is widespread, but its long-term adverse effects on the heart remain poorly understood. This study showed not only substantial LV but also LA remodeling and dysfunctions in young asymptomatic professional strength athletes reporting a long history of AAS use. Left ventricular hypertrophy and LA enlargement were associated with consistent LV diastolic and systolic dysfunction including twist–untwist mechanics and LA reservoir dysfunction. As in many other pathologic situations, the observed atrial abnormalities might to be associated with adverse events including heart failure, atrial fibrillation, stroke and death (44). In the context of an increasing use of AAS, not also in professional but also in recreational bodybuilders, these results are alarming. Our results underline the usefulness of recent STE strain parameters including LV and LA strains to detect early myocardial dysfunction in this population. As atrial remodeling and dysfunction have been shown to be an independent risk factor for cardiac events, these parameters might help to stratify patients at risk who should benefit from close monitoring.

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Conflict of interest:

The authors report no conflicts of interest. The results of the present study do not constitute endorsement by ACSM. All results presented here are done so clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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