

A Cohort Study on Male Athletes Reveals Cardiovascular Toxic Effects Due to Anabolic Androgenic Steroids Abuse

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Abstract

Background: The side effects of abusing anabolic steroids in the cardiovascular system, hepatobiliary system, and endocrinal system exceed the benefits of using them for bodybuilders. Our research assessed the toxicity of anabolic androgenic steroids on cardiac muscles in male athletes. **Methods:** The research was conducted on: Group (A) as a control (46 athletes), Group (B) Athletes taking (Testosterone: Undecanoate) low dose 250 mg/ml (23 athletes) (C) Athletes taking (Testosterone: Undecanoate) high dose 500 mg/ml (23 athletes). Heart rate was calculated manually and confirmed using ECG; QT interval was measured from the beginning of the QRS complex to the end of the T wave and averaged over 3 to 5 beats and QT corrected according to the Bazett formula. Ambulatory blood pressure monitoring allows blood pressure (BP) readings to be recorded over 24 hours giving the day and night SBP (Systolic blood pressure) and DBP (Diastolic blood pressure). Transthoracic echocardiography was performed. Biochemical analysis of HbA1C and lipid profile was performed. **Results:** There were statistically significant differences regarding the day and night blood pressure. Also, there was a statistically significant difference regarding heart rate, QTc, ejection fraction, and left ventricular mass index. There was a significant elevation in Serum Cholesterol, Triglycerides, and LDL (Low-density lipoproteins) levels. There was a significant decrease in serum HDL (high-density lipoproteins) levels. **Conclusions:** All these side effects confirm that abusing anabolic steroids not only has adverse effects but also has life-threatening effects on the heart.

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Key words

Cardiovascular toxicity, Anabolic Androgenic Steroids, Male Athletes Echocardiography

Introduction

During the 21st century the use of anabolic steroids (AS) has become very common among the populations of many countries. The term AS is usually related to the natural testosterone and its synthetic derivatives which are abused by many people to enhance the muscle strength and growth (McVeigh and Begley, 2017). Then testosterone was isolated, and its characteristics were recognized, and this helped to synthesize many derivatives with different properties from that of testosterone. These derivatives were known as anabolic androgenic steroids (AAS) or anabolic steroids (AS) but their use was restricted to bodybuilders and professional athletes. Unfortunately, recreational use by non-professional people is increasing and has become more popular (El Osta et al., 2016).

By the year 1956, more than 200 anabolic steroids had been described due to the synthetic variations performed on testosterone to obtain various effects (Nieschlag and Nieschlag, 2014). Nowadays, AAS is widely distributed all over the world, especially in Western countries like the USA, UK, Scandinavia, and Brazil. The prevalence of their abuse is less common in the Middle East, Southeast Asia, Continental Europe, and other Latin American countries. The majority of AAS abusers are male gym clients desiring to obtain a bigger and more muscular

look and they are not competing in any athletic practice or sport (Pope et al., 2012; Sagoe et al., 2015).

Cardiovascular diseases are considered one of the main health problems worldwide and the largest threat to the lives of humans. The lesions of the cardiovascular system vary in AS abusers with different symptoms and signs (Yan et al., 2017).

Anabolic steroids bind to the androgen receptors in the wall of blood vessels increasing vascular calcification. Long-term effects include cell damage with loss of tissue elasticity and induction of fibrotic hyperplasia (Zhu et al., 2016). The atherosclerotic effect of AS is related to disorders in lipid metabolism. Anabolic steroids induce an increase in the level of LDL and decrease the level of HDL this in turn elevates the risk of cerebrovascular disease and coronary artery disease (Achar, et al., 2010). These changes are reversible, and the lipoprotein levels may return to normal levels with stoppage of their use within weeks to months (Samieinasab et al., 2015).

The studies reported hypertension with AS abuse explained this effect by salt and water retention by the kidney and this effect is reversible within 5 – 12 months of cessation of AS use. Another explanation is the atherosclerotic effect on the wall of blood vessels, but hypertension is irreversible in this condition (Liu and Wu, 2019).

Long-term use of AS may be associated with apoptosis in the cardiac myocytes. Even with normal coronary arteries, some individuals suffer from left ventricular hypertrophy and myocardial scarring (Cecchi et al., 2017). This apoptotic effect of AS increases the mitochondrial permeability and release of apoptotic factors like caspase, cytochrome C, and apoptosis-inducing factor (Baumann, et al., 2014).

Cardiac hypertrophy is common in bodybuilders and athletes using AS for long periods. Anabolic steroids stimulate protein synthesis and inhibit its breakdown. Also, they promote myocardial fibroblastic growth and collagen production. Over a long time, this leads to cardiac hypertrophy and may lead to heart failure (Baggish, et al., 2017).

Long-term abuse of AS may be associated with disturbances in the electrical activity of the heart and may show ECG changes like delay in QRS wave, ventricular and supraventricular extrasystoles, and even ventricular fibrillation (Achar, et al., 2010). These effects may be due to the induction of cardiac autonomic disorders increasing the levels of catecholamines. Also, they may affect the dopaminergic and serotonin system (Neto, et al., 2018).

The most life-threatening condition associated with AS abuse is sudden cardiac arrest which in many cases remains unknown. However, many abusers suffered from sudden cardiac arrest and showed cardiac hypertrophy, cardiomyopathy, ventricular dilatation, and myocardial scarring during the autopsy (Lichtenfeld, et al., 2016).

Unfortunately, the AS abusers often use multiple drugs to enhance their effects such as growth hormone to stimulate muscle growth, insulin and thyroid hormones to increase the absorption and metabolism of nutrients. Also, they use diuretics to get rid of the subcutaneous water aiming to obtain a hard look. This drug combination may have a lethal effect (Sagoe, et al., 2015).

Also, AS inhibit catecholamines breakdown by suppressing their re-uptake in the extra neuronal tissues elevating their concentration at receptor sites. With severe exercise, this may lead to a temporary functional disorder increasing the possibility of ventricular tachyarrhythmias and sudden death (Li, et al., 2018).

Methods

The study was a cohort study carried out on 92 adult athletes. All of them were from one of the Beni-Suef governorate gyms from January 2021 to September 2022. All athletes gave informed consent about the study, benefits, and risk factors. They were able to withdraw at any level of study. The study was performed after approval of the Ethical Committee of the Scientific Research Faculty of Medicine, Beni Suf University, Egypt.

The athletes were classified into 3 groups according to the following:

- Group (A): Control group (46 athletes).
- Group (B): Athletes taking anabolic androgenic steroids (Testosterone Undecanoate amp.) low dose

250 mg/ml intramuscular once per week for at least three months (23 athletes).

- Group (C): Athletes taking anabolic androgenic steroids (Testosterone Undecanoate amp.) high dose of 500 mg/ml intramuscular twice per week for at least three months (23 athletes).
 - Inclusion criteria: Age between 18 to 40, only males were included, age was to match controls, and regular training for at least 3 days a week.
 - Exclusion criteria: Athletes who were suffering from any endocrinal disorders, any cardiac disease, diabetes, or hypertension. Also, athletes who were taking any other anabolic steroids other than of our study, and athletes who were on a ketogenic diet.
 - Controls were chosen randomly from other athletes not taking any of the anabolic steroids.

Drugs and chemicals:

- Anabolic Androgenic Steroids:

Testosterone Undecanoate 250 mg/ml (1 ml) oily solution amp ready for intra-muscular injection provided by MEDI TECH Company. While the group with high dose take 2 ampoules instead of one ampoule.

Physical examination: After history taking, body weight and height were measured, and Body Mass Index (BMI) is a person's weight in kilograms divided by the square of height in meters. $BMI = \text{weight (kg)} / \text{Height}^2 (\text{m}^2)$.

Heart rate, QT and QTc: Heart rate calculated manually and confirmed from resting ECG, QT interval measured from the beginning of the QRS complex to the end of the T wave and averaged over 3 to 5 beats, and QT corrected measured according to Bazett formula: $QTc = QT / \sqrt{RR}$

Ejection fraction and E/A ratio:

- Transthoracic echocardiography was performed.
- The E/A ratio is the ratio of the early (E) to late (A) ventricular filling velocities.
- Modified Simpson method (biplane method of disks) is a modality requiring area tracings of LV (Left ventricle) cavity. The American Society of Echocardiography recommends this method for measuring LVEF (Left ventricular ejection fraction). This method requires the measurement of LVEF by tracing the endocardial border in both the apical four-chamber and two-chamber views in end-systole and end-diastole. These tracings eventually divide the LV cavity into a predetermined number of disks (usually 20). Disk volumes are based on the tracings obtained from the study.
- On the left side, the velocity at which the blood moves during this initial action through mitral valve is called the "E" (for early) filling velocity. Early filling is responsible for roughly 80% of total ventricular filling.
- Echocardiography assessment included EF, E/A for diastolic function, left ventricular mass and left ventricular mass index.

Biochemical Analyses:

- 1- HbA1c (glycated hemoglobin): HbA1c were assayed using ELISA plates (Elabscience

Biotechnology Ltd Company, Beijing, China) according to manufacturer's manual.

- 2- **Lipid Profile:** Total Cholesterol, HDL, VLDL (Very low-density lipoprotein) and LDL levels were determined according to the method described after fasting 10 to 12 hours by (Allain, et al., 1974), (Warnick, et al., 2001) and (Nauck, et al., 2002) respectively using the kits supplied by BioSystems S.A., Barcelona, Spain.

Triglycerides levels were determined according to the method described by (Fossati, and Prencipe, 1982) using the triglycerides kits supplied by BioSystems S.A., Barcelona, Spain.

Statistical Analysis:

Analysis of data was performed using SPSS v. 25 (Statistical Package for Social science) for Windows.

Description of variables was presented as follows:

- Description of quantitative variables was in the form of mean, standard deviation (SD) for normally distributed variables.

All variables were explored for normality and showed that they were normally distributed.

- One-way ANOVA test was used to detect the difference between the three groups regarding the scale variables and Tukey post hoc high significant degree was conducted for multiple comparisons between groups.
- Chi Square test (χ^2): For comparison between categorical variables and percentage values.

Pearson's correlation analysis was done to evaluate linear relationship between studied parameters in anabolic steroids groups. Correlation graphs were drawn only for significant correlation which is considered significant at $P < 0.05$. Correlation is considered positive (direct correlation) when r (correlation coefficient) had a + signal and negative (inverse correlation) in case of - signal and it is considered:

- Weak when $r = >0 - 0.35$,
- Moderate when $r = >0.35 - 0.65$; and
- Strong when $r = > 0.65$.
- The significance of the results was assessed in the form of P-value that was differentiated into:
 - Non-significant when $P\text{-value} > 0.05$.
 - Significant when $P\text{-value} \leq 0.05$.

Results

Age, Weight and Height in different studied groups:

Table 1 showed the comparison in different studied groups according to age, weight and height.

Lipid profile changes in the studied groups (Figures 1, 2, 3, 4 and 5):

Serum total Cholesterol level:

Regarding the serum cholesterol levels, Figure (1) showed that there was a significant difference. The highest levels were seen in group C (210.48±33.79) and the lowest levels were in control group (187.39±11.24). The higher the dose of AS the higher the level of cholesterol.

Serum Triglycerides level:

Regarding the serum triglycerides levels, Figure (2) showed that there was a significant difference between the control group and AS groups.

There is no significant difference between both groups of AS (low dose and high dose).

Serum HDL level:

Regarding the serum HDL level, Figure (3) showed that there was a significant difference. The highest levels were seen in group A (66.43±1.22) and the lowest levels were in group C (46.17±7.23).

Serum LDL level:

Regarding the serum LDL level, Figure (4) showed that there was a significant difference. The highest levels were seen in group C (146.48±32.33) and the lowest levels were in group A (113.04±15.93).

Serum VLDL level:

Regarding the serum VLDL levels, Figure (5) showed that there was a significant difference between the control and AS groups and there is no significant difference between both groups of AS (low dose and high dose). VLDL is significantly higher in control group (25.68±4.22).

Serum HbA1c Level:

Regarding the HbA1c level, Figure (6) showed that there was a significant difference. The highest levels were seen in group C (5.94±0.63) while the lowest levels were seen in group A (5.05±0.24).

Blood pressure and heart rate changes in the studied groups (Tables 2, 3 and 4 – Figures 7 and 8):

- Day blood pressure:

Table (2) and figure (7) showed that there was a statistically significant differences between the control group and AS groups regarding day blood pressure. There is no significant difference between both groups of AS (low dose and high dose). Day blood pressure was significantly lower in control group for both systolic (115.93±5.12) and diastolic (68.76±4.54) blood pressure.

- Night blood pressure:

Table (3) and figure (8) showed that there was a statistically significant differences between the control group and AS groups regarding night blood pressure. There is no significant difference between both groups of AS (low dose and high dose). Night blood pressure was significantly lower in control group for both systolic (110.87±4.76a) and diastolic (66.39±3.90) blood pressure.

- Heart rate:

Table (4) showed that there was a statistically significant differences between the control group and AS groups regarding heart rate ($P\text{-value} < 0.001$). There is no significant difference between both groups of AS (low dose and high dose). Heart rate was significantly lower in the control group A (75.07±8.84) compared to group B (91.87±14.99) and group C (95.70±17.74).

ECG and Transthoracic Echocardiography in studied groups (Tables 5, 6, 7 and 8):

- QT corrected:

Table (5) showed that there was a significant difference between the control group and AS groups regarding QTc. There is no significant difference between both groups of AS (low dose and high dose). QTc was significantly shorter in control (379.78±16.61).

- Ejection fraction (Systolic function):
Regarding the ejection fraction, Table (6) showed that there was a significant difference in different studied groups. The highest ejection fractions were seen in group A (60.09±4.26) while the lowest ejection fractions were seen in group C (51.61±3.16).

- E/A ratio (Diastolic function):
Regarding E/A ratio, Table (7) showed that there was a significant difference. The highest levels were seen in group A (2.01±0.18) while the lowest levels were seen in group C (1.41±0.52).

- Left ventricular mass:
Table (8) showed that there was a significant difference between the control group and AS groups regarding left ventricular mass. There is no significant difference between both groups of AS (low dose and high dose). Left ventricular mass was significantly lower in control (151.74±25.88).

Figure (9) showed that there was a statistically significant weak negative correlation ($r = -0.558$) between E/A ratio and heart rate in low dose group.

Figure (10) showed that there was a statistically significant weak negative correlation ($r = -0.576$)

between left ventricular mass index and weight in High dose group.

Figure (11) showed that there was a statistically significant weak negative correlation ($r = -0.592$) between left ventricular mass index and Body surface area in High dose group.

Table (9) showed no correlation between any parameter of lipid profile in low dose group.

Figure (12) showed that there was a statistically significant weak negative correlation ($r = -0.456$) between left ventricular mass index and cholesterol levels in High dose group.

Figure (13) showed that there was a statistically significant weak negative correlation ($r = -0.437$) between left ventricular mass index and HDL levels in High dose group.

Figure (14) showed that there was a statistically significant weak positive correlation ($r = 0.414$) between left ventricular mass index and LDL levels in High dose group.

Figure (15) showed that there was a statistically significant weak negative correlation ($r = -0.427$) between left ventricular mass index and Non-HDL levels in High dose group.

Table (1): Distribution of age, weight, and height of the studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom were taking anabolic androgenic steroids in different doses.

	Group A	Group B	Group C
Age (Y) (mean ± SD)	25.37±3.88	24.04±2.75	25.78±3.15
P-value	0.197* (NS)		
	Group A	Group B	Group C
Weight (Kg) (mean ± SD)	81.09±7.75	81.17±6.10	85.00±7.60
P-value	0.095* (NS)		
	Group A	Group B	Group C
Height (m) (mean ± SD)	1.73±0.08	1.75±0.04	1.72±0.05
P-value	0.285* (NS)		

Table (2): Comparison between studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom took the anabolic androgenic steroids at different doses in relation to daily blood pressure.

	Group A	Group B	Group C	P-value
SBP (day) mm.Hg mean ± SD	115.93±5.12 ^a	127.70±4.30 ^b	130.30±6.24 ^b	<0.001*
DBP (day) mm.Hg mean ± SD	68.76±4.54 ^a	78.13±4.61 ^b	80.30±5.69 ^b	<0.001*

* P -value ≤ 0.05 is considered significant by (ANOVA). Means with different superscripts letters (^a, ^b) in the same row are significantly different at ($p \leq 0.05$)

Table (3): Comparison between the studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom were taking anabolic androgenic steroids in different doses as regards night blood pressure.

	Group A	Group B	Group C	P-value
SBP (night) mm.Hg mean ± SD	110.87±4.76 ^a	115.26±5.01 ^b	121.52±5.71 ^b	<0.001*
DBP (night) mm.Hg mean ± SD	66.39±3.90 ^a	67.83±4.23 ^a	71.65±5.88 ^b	<0.001*

* P -value ≤ 0.05 is considered significant by (ANOVA). Means with different superscripts letters (^a, ^b) in the same row are significantly different at ($p \leq 0.05$)

Table (4): Comparison between the studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom were taking anabolic androgenic steroids in different doses as regards heart rate.

	Group A	Group B	Group C
Heart rate(beat/min) mean \pm SD	75.07 \pm 8.84 ^a	91.87 \pm 14.99 ^b	95.70 \pm 17.74 ^b
P-value	<0.001*		

* P-value \leq 0.05 is considered significant by (ANOVA). Means with different superscripts letters (^a, ^b) in the same row are significantly different at ($p \leq 0.05$)

Table (5): Comparison between the studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom were taking anabolic androgenic steroids in different doses in relation to QTc.

	Group A	Group B	Group C
QTc mean \pm SD	379.78 \pm 16.61 ^a	398.87 \pm 17.65 ^b	404.26 \pm 17.32 ^b
P-value	<0.001*		

* P-value \leq 0.05 is considered significant by (ANOVA). Means with different superscripts (a, b) letters in the same row are significantly different at ($p \leq 0.05$)

Table (6): Comparison between the studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom were taking anabolic androgenic steroids in different doses as regards ejection fraction.

	Group A	Group B	Group C
Ejection fraction % mean \pm SD	60.09 \pm 4.26 ^c	54.30 \pm 5.16 ^b	51.61 \pm 3.16 ^a
P-value	<0.001*		

* P-value \leq 0.05 is considered significant by (ANOVA). Means with different superscripts letters (^a, ^b, ^c) in the same row are significantly different at ($p \leq 0.05$)

Table (7): Comparison between the studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom were taking anabolic androgenic steroids in different doses as regards E/A ratio:

	Group A	Group B	Group C
E/A ratio mean \pm SD	2.01 \pm 0.18 ^c	1.77 \pm 0.50 ^b	1.41 \pm 0.52 ^a
P-value	<0.001*		

* P-value \leq 0.05 is considered significant by (ANOVA). Means with different superscripts letters in the same row are significantly different at ($p \leq 0.05$)

Table (8): Comparison between the studied adult athletes who went to a gym from January 2021 to September 2022 and some of whom were taking anabolic androgenic steroids in different doses as regards left ventricular mass:

	Group A	Group B	Group C	P-value
Left ventricular mass	151.74 \pm 25.88 ^a	221.22 \pm 35.16 ^b	228.00 \pm 39.13 ^b	<0.001*

* P-value \leq 0.05 is considered significant by (ANOVA). Means with different superscripts letters (^a, ^b) in the same row are significantly different at ($p \leq 0.05$)

Correlations

Table (9): Correlations of echocardiographic measurements and lipid profile of low dose (250 mg) anabolic steroid users (n=23).

	Left ventricular mass	left ventricular mass index	E/A ratio
Cholesterol (mg/dl)	r = -0.064	r = -0.039	r = -0.277
Triglycerides (mg/dl)	r = -0.109	r = -0.103	r = -0.053
HDL (mg/dl)	r = -0.095	r = -0.049	r = -0.175
LDL (mg/dl)	r = -0.028	r = -0.007	r = -0.189
VLDL	r = -0.143	r = -0.088	r = -0.009
Non-HDL	r = -0.047	r = -0.019	r = -0.191

No correlation between any parameter of lipid profile in low dose group. Pearson's correlation coefficient was determined.

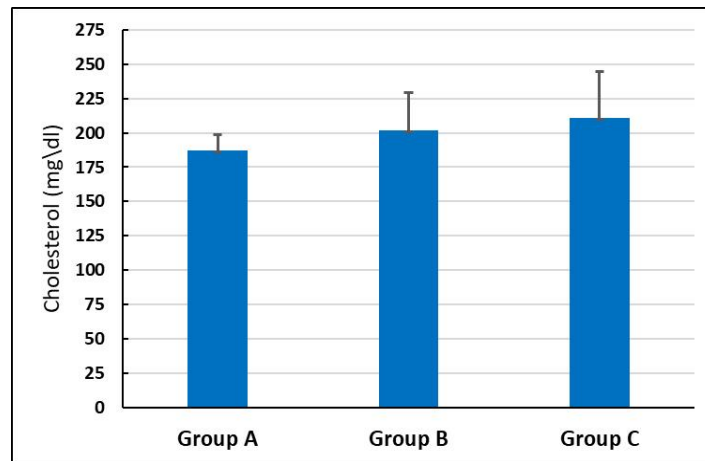


Figure (1): Distribution of serum cholesterol level among the studied groups

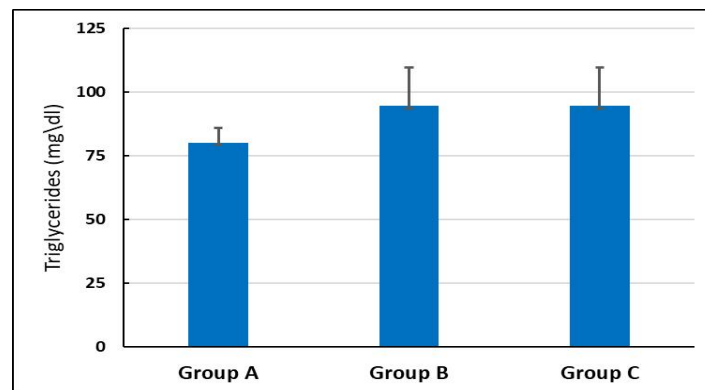


Figure (2): Distribution of serum triglycerides level among the studied groups.

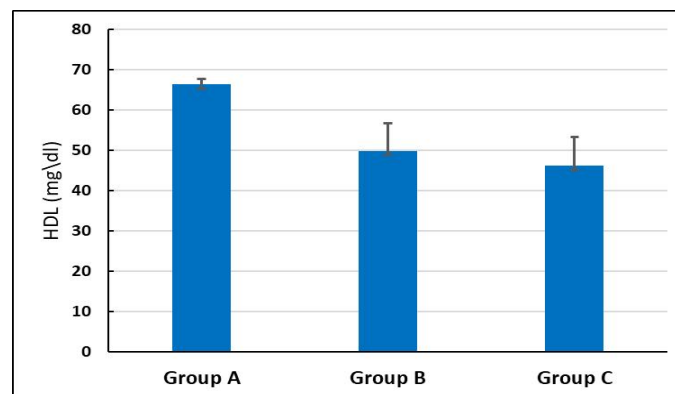


Figure (3): Distribution of serum HDL level among the studied groups.

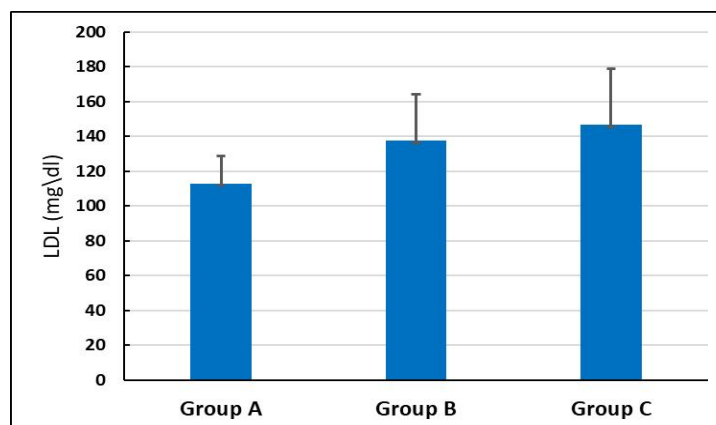


Figure (4): Distribution of serum LDL level among the studied groups.

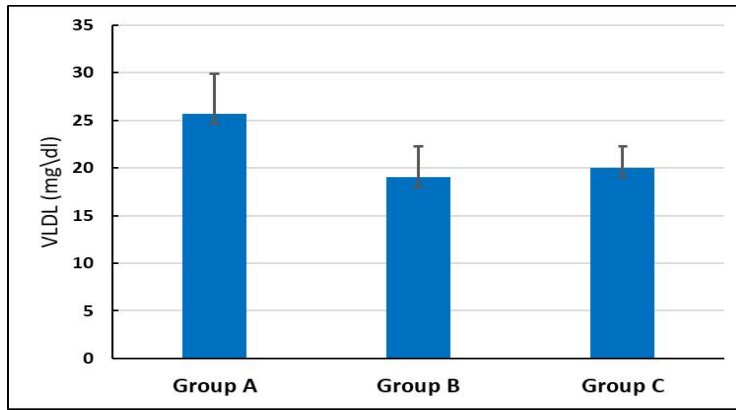


Figure (5): Distribution of serum VLDL level among the studied groups.

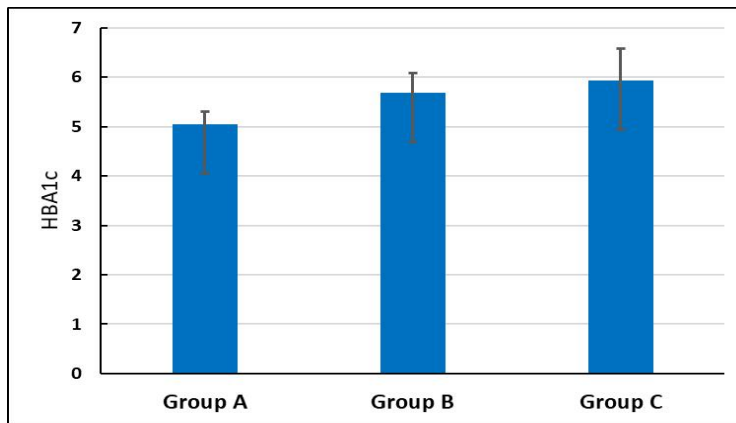


Figure (6): Distribution of HbA1c level among the studied groups.

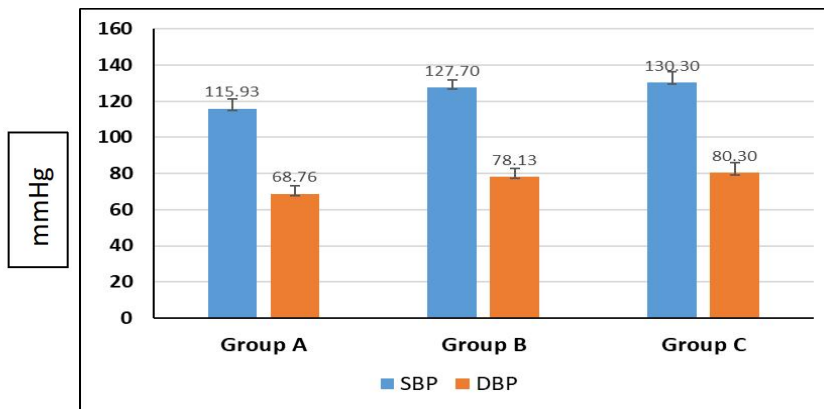


Figure (7): Distribution of day blood pressure among the studied groups.

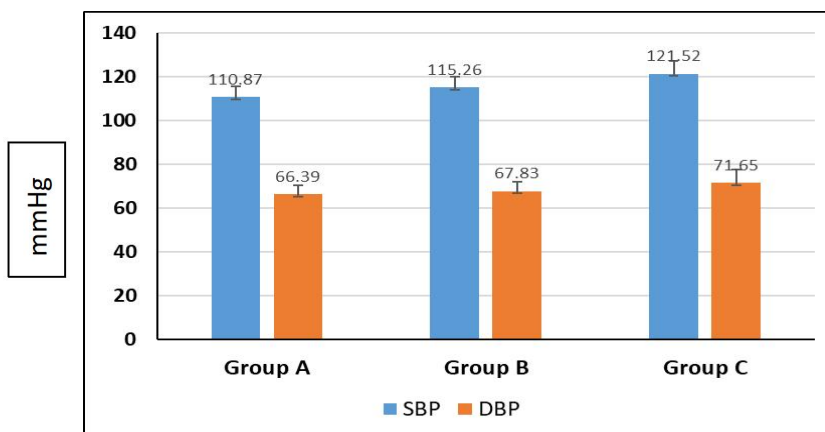


Figure (8): Distribution of night blood pressure among the studied groups.

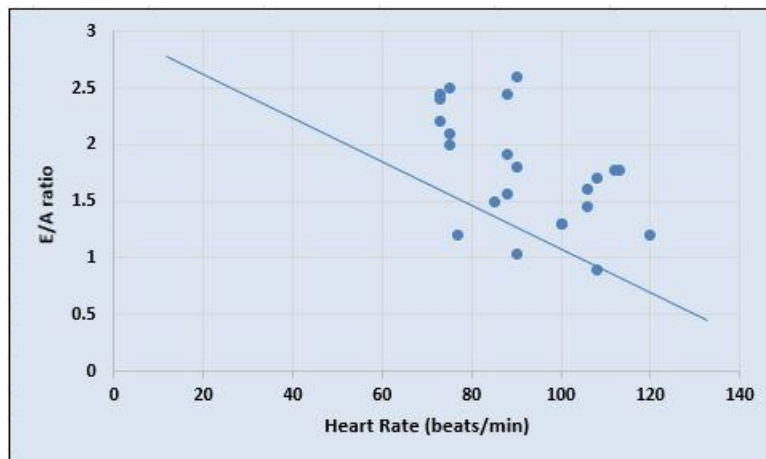


Figure (9): relation between E/A ratio and heart rate in low dose group ($r = -0.558^{**}$).

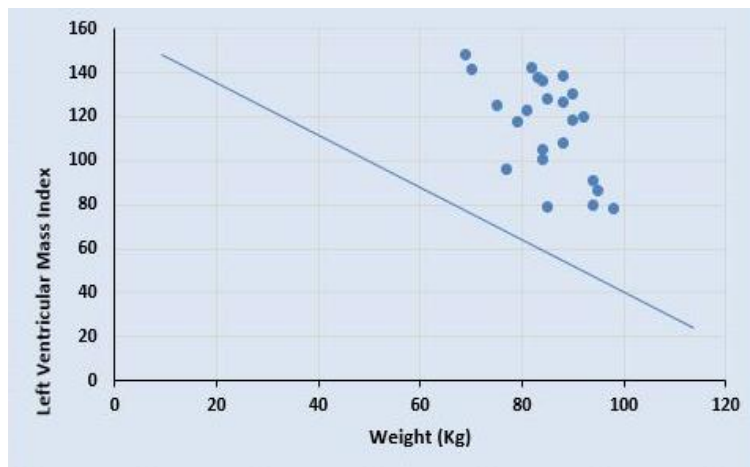


Figure (10): relation between left ventricular mass index and weight in high dose group ($r = -0.576^{**}$).

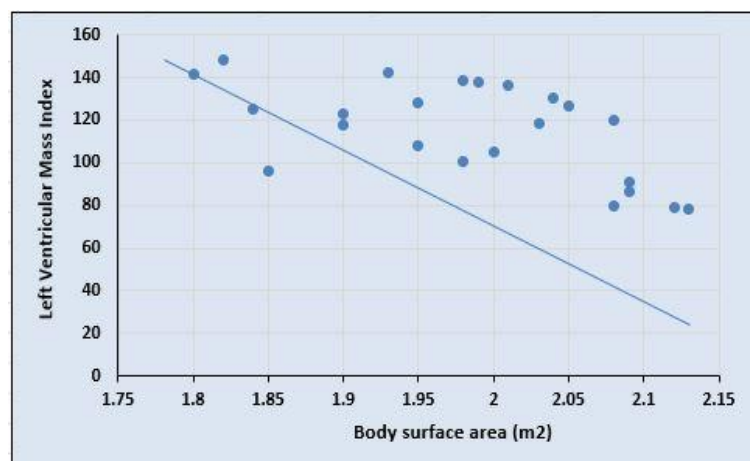


Figure (11): relation between left ventricular mass index and Body surface area in high dose group ($r = -0.592^{**}$).

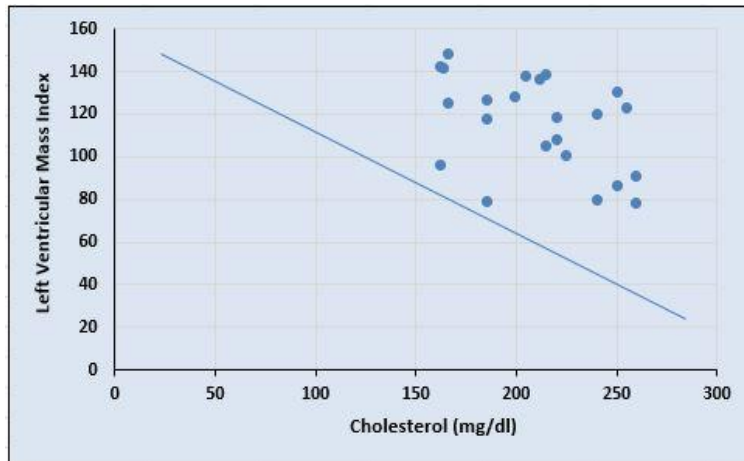


Figure (12): Relation between left ventricular mass index and cholesterol levels in high dose group ($r = -0.456^*$).

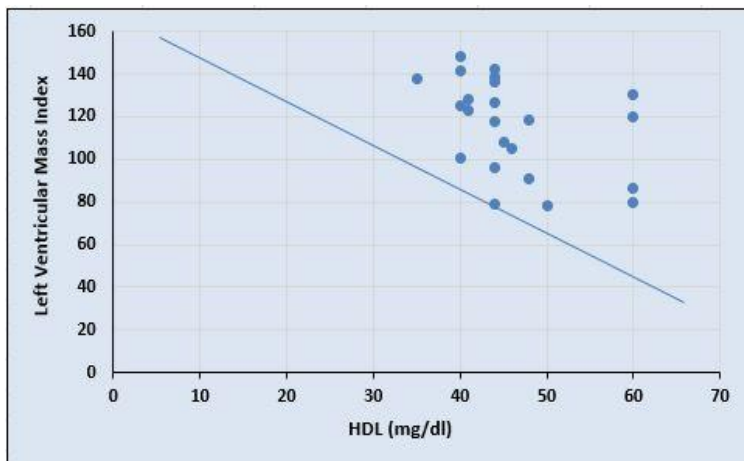


Figure (13): Relation between left ventricular mass index and HDL levels in high dose group ($r = -0.437^*$).

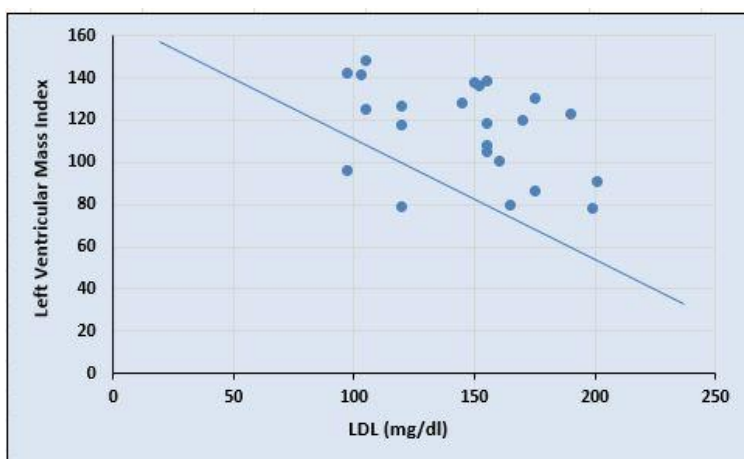


Figure (14): Relation between left ventricular mass index and LDL levels in high dose group ($r = 0.414^*$).

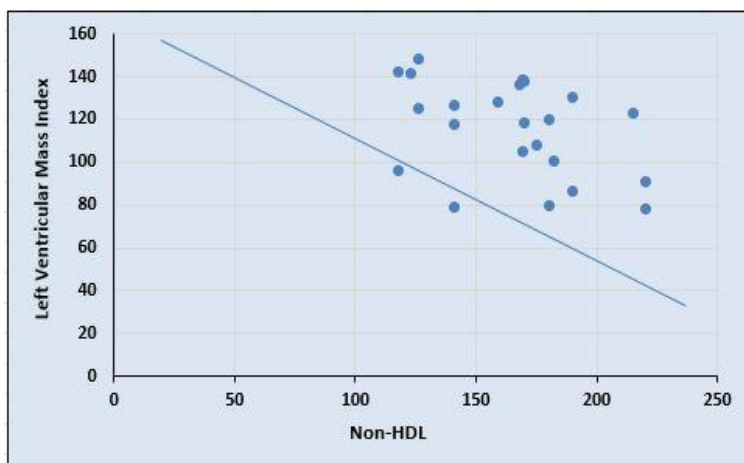


Figure (15): Relation between left ventricular mass index and Non-HDL levels in high dose group ($r = -0.427^*$).

Discussion

The use of AAS has increased recently by young adults especially athletes and bodybuilders aiming to improve their self-esteem by having a better appearance through increasing their body mass and weight. But toxicity effects were reported with the AAS abuse (Tasgin, et al., 2011)

The present study was conducted to evaluate the toxicity induced by anabolic androgenic steroids on some cardiovascular parameters. The mean age of cases receiving AS at low dose was 24.04 ± 2.75 with an average BMI of 26.58 ± 2.37 and body surface area of 1.97 ± 0.07 and those with high dose had an average age of 25.78 ± 3.15 , BMI of 28.65 ± 2.58 , and body surface area 1.98 ± 0.10 . There were no significant differences between all groups as regards their age, weight, height, BMI, and body surface area.

Dyslipidemia is considered a major risk factor for IHD and CVD. Compared to the control group, athletes on AS showed a significant elevation in serum cholesterol, triglycerides, and LDL levels. On the other hand, there was a significant decrease in serum HDL levels. There was a significant elevation in serum cholesterol, VLDL, and LDL levels in the high-dose group compared to the low-dose group, while there was no significant difference in triglycerides.

Several studies evaluated the effect of anabolic steroids on lipid profile. The study of (Liu, and Wu, 2019) about anabolic steroids use and CVS risks run in parallel with our results and demonstrated that AS use correlates with an increase of LDL in serum and decreases HDL levels in serum.

Also, the study of Rosca, et al., (2019) about the changes in lipid profile associated with chronic use of anabolic steroids affirmed an increase in triglycerides and LDL with a decrease in HDL in plasma. In contrary to our study was Gheshlaghi, et al., (2015) in their study of cardiovascular manifestations caused by chronic anabolic steroids use who found a decrease in LDL and no changes in HDL levels in plasma. However, this study was limited to a short period of two months among a small group of 267 athletes.

The abuse of AS in supra-physiological doses is strongly associated with abnormal levels of plasma

lipoproteins showed a decreased level of HDL and increased levels of LDL and cholesterol levels (Albano, et al., 2021)

A 24 hours ambulatory blood pressure and HR were conducted to assess the effect of AS on the CVS. Our study revealed that, there were statistically significant differences between the control group, and AS groups regarding the day and night blood pressure while, there was no significant difference between both groups of AS (low and high doses). Night blood pressure was significantly lower in control group for both systolic and diastolic. Systolic blood pressure was (110.87 ± 4.76 and 115.93 ± 5.12 mmHg) for night and day respectively, while the diastolic BP was (66.39 ± 3.90 and 68.76 ± 4.54 mmHg) for night and day times respectively.

Also, there was a statistically significant difference between the control group and AS groups as regards heart rate while, there was no significant difference between both groups of AS (low dose and high dose). Heart rate was significantly lower in control group with mean \pm SD (75.07 ± 8.84 beat/min).

In agreement with our study was the study of Grandperrin et al., (2022) about the alteration on myocardial work in athletes with AS use who revealed that the mean systolic blood pressure was 127 ± 8 mmHg, and the mean diastolic blood pressure was 77 ± 8 mmHg however, the mean heart rate was 68 ± 11 beat/minute.

Similarly, the study of Angell, et al., (2018) about acute cardiovascular response in AS users showed that the HR (bpm) increased to 84 ± 1 after AS use, systolic BP (mm/Hg) increased to 134 ± 14 and diastolic BP (mm/Hg) increased to 74 ± 11 after the use of anabolic steroids.

The relation between AAS abuse and blood pressure is controversial. A link between AAS abuse and elevated blood pressure has been observed in the study of Urhausen, et al., (2004) whereas the study of D'Andrea, et al., (2006) and that of Lane, et al., (2006) showed no association. When hypertension is observed, it likely follows renal retention of sodium from AAS.

Imaging of the cardiac tissue was performed by ECG and echocardiography. ECG of cases under the study demonstrated that there was a statistically significant difference between the control group and AS groups regarding QTc while, there was no significant difference between both groups of AS (low dose and high dose). QTc was significantly shorter in control group with mean \pm SD (379.78 \pm 16.61).

Echocardiography assessment included EF, E/A for diastolic function, left ventricular mass and left ventricular mass index. Our study showed that as regards to the EF and E/A ratio, there was a significant difference between all groups. The control group showed the highest levels in both EF and E/A ratio (60.09 \pm 4.26), (2.01 \pm 0.18) while the high dose group showed the lowest levels in both EF and E/A ratio (51.61 \pm 3.16), (1.41 \pm 0.52).

As regards to the left ventricular mass, there was a significant difference between the control group and AS groups. While, there was no significant difference between both groups of AS (low dose and high dose). Left ventricular mass was significantly lower in control (151.74 \pm 25.88).

In consistency with our study was that (Fykse, et al., 2022) who evaluated the long-term effects of anabolic steroids on the cardiovascular system and revealed that the echocardiography changes were a decrease in the EF to 50%, the LV mass increased to 254 and the LV mass index increased to 112.

The study of (Torrise, et al., 2020) on the ECG changes induced by AS showed alterations in myocardial electrophysiology such as significantly longer QTc interval and greater QT dispersion, at rest and after moderate exercise.

However, unlike our study (Puppin, et al., 2019) assessed the impact of anabolic steroids abuse and didn't observe any changes in the ECG among study participants.

Continuous use of blood glucose monitors is becoming more common. HbA1c is measured primarily to determine the three-month average blood sugar level and can be used as a diagnostic test for diabetes mellitus and as an assessment test for glycemic control in people with diabetes (Manley, et al., 2004).

In this study as regards to the HbA1c level, there was a significant difference between all groups. The highest levels were seen in high dose group (5.94 \pm 0.63) while the lowest levels were seen in control group (5.05 \pm 0.24).

This result matched with (Bilgin, et al., 2020) reported a marked increase in the serum HbA1c with athletes who received Anabolic steroids. While (Lykhanov and Babenko, 2018) who studied the effect of anabolic steroids on glucose metabolism and showed a shift in all glucose metabolism rates closer to the upper normal values in athletes after stopping the use of anabolic androgenic steroids.

Conclusion and Recommendations

According to AS effect on blood pressure, the study showed a significant elevation of both systolic and diastolic blood pressure during day and night. Also,

these effects on 24 hours blood pressure more prominent in higher doses of anabolic steroids rather than small dose.

Anabolic steroid has effect also on endocrine system. The use of AS (high dose and low dose) showed elevation in HbA1c compared to the control group. This study confirms diabetogenic effect of anabolic steroids.

ECG showed different parameter, decreasing in both systolic and diastolic function of the heart and increasing heart rate during rest and a prolonged QTc.

Echocardiography also showed significant increase in both left ventricular mass and left ventricular mass index in abuser of Anabolic steroids (high and low doses) compared to control group.

All these side effects confirm that abusing of anabolic steroids not only have adverse effect but also have life-threatening effect on heart.

Our recommendations are: Increasing the awareness by the hazards of anabolic steroids abusing for non-medical indication, Supervision on gyms to prevent illegal trade and prescription of anabolic steroids by non-specialist, Regular Echo assessment, ECG and cardiac enzymes for them, Further studies should be done on herbal plants and naturally occurring protective substances and Further studies should be applied on people who stopped using anabolic steroid to know the reversible and non-reversible toxic effects of anabolic steroids.

References

- Achar S; Rostamian A and Narayan S M (2010): Cardiac and metabolic effects of anabolic-androgenic steroid abuse on lipids, blood pressure, left ventricular dimensions, and rhythm. *The American journal of cardiology*, 106 (6): 893-901.
- Albano G D; Amico F; Cocimano G; Liberto A; Maglietta F; Esposito M; Rosi GL; Di Nunno N; Salerno M and Montana A (2021): January. Adverse Effects of Anabolic-Androgenic Steroids: A Literature Review. In *Healthcare: Multidisciplinary Digital Publishing Institute*, 9 (1): 97.
- Allain C C.; Poon L S; Chan C S; Richmond W F P C and Fu P C (1974): Enzymatic determination of total serum cholesterol. *Clinical chemistry*, 20 (4): 470-475.
- Angell P J, Green D J, Lord R, Gaze D, Whyte G, and George K. P (2018): Acute cardiovascular responses to resistance exercise in anabolic steroids users: A preliminary investigation. *Science & Sports*. doi: 10.1016/j.scispo.2018.05.003
- Baggish A L; Weiner R B; Kanayama G; Hudson J I; Lu M T; Hoffmann U and Pope Jr H G (2017): Cardiovascular toxicity of illicit anabolic-androgenic steroid use. *Circulation*, 135 (21): 1991-2002.
- Baumann S; Jabbour C; Huseynov A; Borggreffe M; Haggi D and Papavassiliu T (2014): Myocardial scar detected by cardiovascular magnetic resonance in a competitive bodybuilder with

- longstanding abuse of anabolic steroids. *Asian journal of sports medicine*, 5 (4): 24058.
- Bilgin S, Aktas G, Zahid Kocak M, Atak B M, Kurtkulagi O, Duman T T, and Savli H (2020): Association between novel inflammatory markers derived from hemogram indices and metabolic parameters in type 2 diabetic men. *The Aging Male*, 23(5), 923-927.
- Cecchi R; Muciaccia B; Ciallella C; Di Luca N M; Kimura A; Sestili C; Nosaka M and Kondo T (2017): Ventricular androgenic-anabolic steroid-related remodeling: an immunohistochemical study. *International journal of legal medicine*, 131 (6): 1589-1595.
- D'Andrea A, Caso P, Salerno G, Scarafile R, De Corato G, Mita C, Di Salvo G, Severino S, Cuomo S, Liccardo B and Esposito N. (2006): Left ventricular early myocardial dysfunction after chronic misuse of anabolic androgenic steroids: a Doppler myocardial and strain imaging analysis. *British journal of sports medicine*, 41(3), pp.149-155.
- El Osta R, Almont T, Diligent C, Hubert N, Eschwège P and Hubert J, (2016): Anabolic steroids abuse and male infertility. *Basic and clinical andrology*, 26 (1): 2. doi: 10.1186/s12610-016-0029-4
- Fossati P and Prencipe L (1982): Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clinical chemistry*, 28 (10): 2077-2080.
- Fykse T S, Vanberg P, Gjesdal K., von Lueder T G, Bjørnerheim R, Steine K., Atar D and Halvorsen S, (2022): Cardiovascular phenotype of long-term anabolic-androgenic steroid abusers compared with strength-trained athletes. *Scandinavian Journal of Medicine & Science in Sports*.
- Gheshlaghi F, Piri-Ardakani M R, Masoumi G R, Behjati M, and Paydar P (2015): Cardiovascular manifestations of anabolic steroids in association with demographic variables in body building athletes. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, 20(2), 165.
- Grandperrin A, Schnell F, Donal E, Galli E, Hedon C, Cazorla O, and Nottin S (2022): Specific alterations of regional myocardial work in strength-trained athletes using anabolic steroids compared to athletes with genetic hypertrophic cardiomyopathy. *Journal of Sport and Health Science*.
- Lane H A, Grace F, Smith J C, Morris K., Cockcroft J, Scanlon M F, and Davies J S (2006): Impaired vasoreactivity in bodybuilders using androgenic anabolic steroids. *European journal of clinical investigation*, 36(7), 483-488.
- Li C; Adhikari BK.; Gao L; Zhang S; Liu Q; Wang Y and Sun J (2018): Performance-enhancing drugs abuse caused cardiomyopathy and acute hepatic injury in a young bodybuilder. *American journal of men's health*, 12 (5): 1700-1704.
- Lichtenfeld J; Deal B J and Crawford S (2016): Sudden cardiac arrest following ventricular fibrillation attributed to anabolic steroid use in an adolescent. *Cardiology in the Young*, 26 (5): 996.
- Liu J D and Wu Y Q, (2019): Anabolic-androgenic steroids and cardiovascular risk. *Chinese medical journal*, 132(18), pp.2229-2236.
- Lykhonosov M P, and Babenko A Y (2018): Some Indicators of Carbohydrate Metabolism in Individuals after the Abolition of the Use of Anabolic Androgenic Steroids. *Diabetes*, 67(Sup_1).
- Manley S, John WG, Marshall S (July 2004): "Introduction of IFCC reference method for calibration of HbA: implications for clinical care". *Diabet. Med.* 21 (7): 673-676. doi:10.1111/j.1464-5491.2004.01311.x. PMID 15209757. S2CID 30468208.
- McVeigh J and Begley E (2017): Anabolic steroids in the UK: an increasing issue for public health. *Drugs: Education, Prevention and Policy*, 24 (3): 278-285.
- Nauck M; Warnick GR and Rifai N (2002): Methods for measurement of LDL-cholesterol: a critical assessment of direct measurement by homogeneous assays versus calculation. *Clinical chemistry*, 48 (2): 236-254.
- Neto O B; da Mota G R; De Sordi C C; Resende E A M; Resende L A P; da Silva M A V ; Marocolo M; Côrtes R S; de Oliveira L F and da Silva V J D (2018): Long-term anabolic steroids in male bodybuilders induce cardiovascular structural and autonomic abnormalities. *Clinical Autonomic Research*, 28 (2): 231-244.
- Nieschlag E and Nieschlag S, (2014): Testosterone deficiency: a historical perspective. *Asian journal of andrology*, 16 (2): 161-8, doi: 10.4103/1008-682X.122358.
- Pope Jr H G, Kanayama G and Hudson J I, (2012): Risk factors for illicit anabolic-androgenic steroid use in male weightlifters: a cross-sectional cohort study. *Biological psychiatry*, 71 (3): 254-261.
- Puppim C G C, Moraes F D S., Gomes L R R, do Nascimento A M , de Lima E M, Brasil G A, Bissol, N S, Lenz D, Endringer D C and de Andrade T U (2019): Anabolic androgenic steroid users: a tilt test study with young adult men. *Archives of Medical Science-Civilization Diseases*, 4(1), pp.75-83.
- Rosca A E, Stancu C S, Badiu C, Popescu B.O, Mirica R, Căruntu C, and Zagrean A M (2019): Lipid profile changes induced by chronic administration of anabolic androgenic steroids and taurine in rats. *Medicina*, 55(9), 540.
- Sagoe D; McVeigh J; Bjørnebekk A.; Essilfie M S; Andreassen C S and Pallesen S (2015): Polypharmacy among anabolic-androgenic steroid users: a descriptive metasynthesis. *Substance Abuse Treatment, Prevention, and Policy*, 10 (1): 1-19.
- Samieinasab M R; Shahraki M R; Samieinasab F and Najafi S (2015): Influence of nandrolone decanoate administration on serum lipids and

- liver enzymes in rats. ARYA atherosclerosis, 11 (4): 256.
- Tasgin E; Lok S and Demir N (2011): Combined usage of testosterone and nandrolone may cause heart damag. African Journal of Biotechnology, 10 (19): 3766-3768.
- Torrisi M, Pennisi G, Russo I, Amico F, Esposito M, Liberto A, Cocimano G, Salerno M, Li Rosi G, Di Nunno N and Montana A, (2020): Sudden cardiac death in anabolic-androgenic steroid users: a literature review. Medicina, 56(11), p.587.
- Urhausen A, Albers T, & Kindermann W (2004): Are the cardiac effects of anabolic steroid abuse in strength athletes reversible?. Heart, 90(5), 496-501.
- Warnick G R; Nauck M and Rifai N (2001): Evolution of methods for measurement of HDL-cholesterol: from ultracentrifugation to homogeneous assays. Clinical chemistry, 47 (9): 1579-1596.
- Yan R; Li W; Yin L; Wang Y; Bo J; PURE-China Investigators; Liu L; Liu B; Hu B and Chen C (2017): cardiovascular diseases and risk-factor burden in urban and rural communities in high-, middle-, and low-income regions of China: a large community-based epidemiological study. Journal of the American Heart Association, 6 (2): 4445. doi: 10.1161/JAHA.116.004445.
- Zhu D; Hadoke P W; Wu J; Vesey A T; Lerman D A; Dweck M R; Newby D E; Smith L B and MacRae V E (2016): Ablation of the androgen receptor from vascular smooth muscle cells demonstrates a role for testosterone in vascular calcification. Scientific reports, 6 (1): 1-3.
- دراسة على الرياضيين الذكور تكشف التأثيرات السامة على القلب والأوعية الدموية بسبب تعاطي المنشطات الأندروجينية الابتنائية**

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الملخص العربي

الخلفية: الآثار الجانبية لتعاطي المنشطات في نظام القلب والأوعية الدموية، ونظام الكبد الصفراوي ونظام الغدد الصماء تتجاوز فوائد استخدامها للاعبين كمال الأجسام. قام بحثنا بتقييم سمية المنشطات الأندروجينية الابتنائية على عضلات القلب لدى الرياضيين الذكور.

الطرق: أجري البحث على: المجموعة (أ) كمجموعة ضابطة (46 رياضياً). المجموعة (ب) الرياضيون الذين يتناولون (Testosterone Undecanoate) بجرعة منخفضة 250 ملغم/مل (23 رياضياً) (ج) الرياضيون الذين يتناولون (Testosterone Undecanoate) جرعة عالية 500 ملغم/مل (23 رياضي). يتم حساب معدل ضربات القلب يدوياً وتأكيده من تخطيط كهربية القلب أثناء الراحة، وقياس فترة QT من بداية مجمع QRS إلى نهاية موجة T ومتوسطها أكثر من 3 إلى 5 نبضة وقياس QT المصحح. تسمح مراقبة ضغط الدم المتنقلة بتسجيل قراءات ضغط الدم (BP) على مدار 24 ساعة مع تحديد اليوم والقریب SBP و DBP. تم إجراء تخطيط صدى القلب عبر الصدر.

النتائج: كان هناك ارتفاع كبير في مستويات الكوليسترول في الدم والدهون الثلاثية ومستويات LDL كان هناك انخفاض كبير في مستويات HDL في الدم. وكانت هناك فروق ذات دلالة إحصائية فيما يتعلق بضغط الدم ليلاً ونهاراً. كما كان هناك فروق ذات دلالة إحصائية فيما يتعلق بمعدل ضربات القلب، QTc، والكسر القذفي ومؤشر كتلة البطين الأيسر. الاستنتاجات: كل هذه الآثار الجانبية تؤكد أن تعاطي الستيرويدات البنائية ليس له آثار ضارة فحسب، بل له أيضاً تأثير مهدد للحياة على القلب.

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