Letter to the Editor

Can AAS-Induced Cardiac Dysfunction Be Reversible?

Dear Editor,

Observational evidence has demonstrated that chronic abuse of anabolic-androgenic steroids (AAS) can lead to significant cardiovascular damage, including left ventricular hypertrophy, systolic and diastolic dysfunction, and progression to severe heart failure [1-3].Conversely, some authors have reported that, following an appropriate diagnosis of cardiomyopathy, cessation of AAS use, and initiation of clinical pharmacological treatment, the deleterious morphological and functional effects may be reversible to normal parameters [4-8].

For instance, Milevski SV. et al. (2022) [4] described a case involving a 46-year-old man diagnosed with severe dilated cardiomyopathy (LVEF 12%) after ten years of prolonged AAS abuse. Six months after discontinuing AAS use and initiating heart failure treatment, combined with testosterone replacement therapy to physiological levels, the patient experienced complete symptom reversal, with LVEF improving to 61%.

In another case report by Doleeb S. et al. (2019) [5], a male bodybuilder with a history of chronic AAS abuse for over three years presented with symptoms of dyspnea, fatigue, palpitations, and syncope at the time of dilated cardiomyopathy diagnosis, along with an LVEF of 12%. Pharmacological treatment for heart failure and cessation of AAS use led to symptom remission and an LVEF recovery to 54% after six months of clinical follow-up.

Comment [d1]: 15%

Comment [d2]: GLS improved but not fully normal

Gul U. et al. (2022) [6] reported a case involving a 47-year-old non-athlete woman who had used supraphysiological doses of AAS over an extended period. She presented with severe pulmonary edema and left ventricular dysfunction (LVEF 34%) at the time of cardiomyopathy diagnosis. Following AAS discontinuation and clinical pharmacological treatment for heart failure, the patient experienced regression of left

ventricular hypertrophy (with no evidence of fibrosis) and an LVEF improvement to 57%, with no residual clinical symptoms.

Additionally, two observational studies [7,8] have also documented that the recovery of morphological and functional parameters (left ventricular hypertrophy and systolic and diastolic dysfunction) may be potentially reversible, reaching values considered normal after cessation of chronic AAS abuse and initiation of pharmacological treatment for heart failure over a period of 6 to 8 months.

Nevertheless, the reversibility of cardiac damage caused by AAS abuse is not universally reported across studies. The systolic (reduced LVEF and longitudinal strain) and diastolic dysfunction (reduced E/A ratio) induced by AAS observed in the study by Baggish AL. et al. (2010) [1] did not resolve even after six months of discontinuation. Similarly, Abdullah R. et al. (2024) [2], evaluating former AAS users six years after cessation, and Rasmussen JJ. et al. (2018) [3], assessing individuals 30 months post-discontinuation, observed persistent left ventricular hypertrophy, reduced LVEF, and impaired global longitudinal strain, suggesting potential permanent cardiac damage.

In summary, substantial evidence indicates that chronic AAS abuse promotes left ventricular hypertrophy and progressive diastolic dysfunction, potentially advancing to severe systolic dysfunction and heart failure [1-3]. While some studies suggest partial or complete reversibility of functional alterations following cessation [4-8], others report persistent damage even years after discontinuation, such as sustained left ventricular hypertrophy and reduced global longitudinal strain [1-3]. These discrepancies may suggest that the extent and persistence of cardiac damage could be related to the cumulative AAS abuse burden (dose and duration), as well as individual factors potentially not captured in observational studies or case reports. This underscores the importance of a close cardiological follow-up, aiming early detection of alterations, and appropriate therapeutic management in individuals exposed to these compounds.

References:

1 - Baggish AL, Weiner RB, Kanayama G, Hudson JI, Picard MH, Hutter AM Jr, et al. Long-term anabolic-androgenic steroid use is associated with left ventricular dysfunction. Circ Heart Fail. 2010 Jul;3(4):472-6. doi: 10.1161/CIRCHEARTFAILURE.109.931063.

however, AAS users had significantly lower LV ejection fraction (50.6% [48.4, 53.6] versus 59.1% [58.0%, 61.7%]; P=0.003 by two-tailed Wilcoxon rank sum test), longitudinal strain (16.9% [14.0%, 19.0%] versus 21.0% [20.2%, 22.9%]; P=0.004), and radial strain (38.3% [28.5%, 43.7%] versus 50.1% [44.3%, 61.8%]; P=0.02). Ten of the 12 AAS users showed LV ejection fractions below the accepted limit of normal (>or=55%). AAS users also demonstrated decreased diastolic function compared to nonusers as evidenced by a markedly lower early peak tissue velocity (7.4 [6.8, 7.9] cm/s versus 9.9 [8.3, 10.5] cm/s; P=0.005) and early-to-late diastolic filling ratio (0.93 [0.88, 1.39] versus 1.80 [1.48, 2.00];
Four of the 12 AAS users were currently taking supraphysiologic doses of AAS at the time of evaluation; three were currently taking only physiologic doses of testosterone at 50–100 mg per week; one had discontinued a course of supraphysiologic AAS three weeks prior to evaluation; and the remaining four had not used AAS for at least six months prior to the evaluation.
Six (50%) of the AAS users, but none of the non-users, reported a past history of opioid, cocaine, or alcohol dependence. None of the participants reported amphetamine dependence. Two (17%) AAS users, but none of the non-users, reported cannabis dependence, one in the past and one current. None of the participants reported a history of cigarette use. Nine (75%) of the AAS users, but none of the non-users, reported at least some use of human growth hormone, and six of these reported human growth hormone use for more than 3 months. We assessed for possible cardiac effects of these other forms of drug use in exploratory analyses as described below.

2 - Abdullah R, Bjørnebekk A, Hauger LE, Hullstein IR, Edvardsen T, Haugaa KH, et al. Severe biventricular cardiomyopathy in both current and former long-term users of anabolic-androgenic steroids. Eur J PrevCardiol. 2024 Mar 27;31(5):599-608. doi: 10.1093/eurjpc/zwad362.

History of amphetamine use (n, (%))	47 (47)a	35 (51)c	12 (40)d	5 (7)
History of cocaine use (n, (%))	49 (49)a	36 (52)c	13 (43)d.	8(11)

In this cross-sectional study, 101 weightlifting AAS users with at least 1 year cumulative AAS use (mean 11 ± 7 accumulated years of AAS use) were compared with 71 non-using weightlifting controls (WLC) using clinical data and echocardiography. Sixty-nine were current, 30 former (>1 year since quitted), and 2 AAS users were not available for this classification. Not about pharmacological treatment

3 - Rasmussen JJ, Schou M, Madsen PL, Selmer C, Johansen ML, Ulriksen PS, et al. Cardiac systolic dysfunction in past illicit users of anabolic androgenic steroids. Am Heart J. 2018 Sep;203:49-56. doi: 10.1016/j.ahj.2018.06.010.

Cardiac ***MRI*** **showed similar pattern of group-differences in LVEF as echocardiography, being decreased in the group of current AAS abusers compared with the other two groups,** P < 0.001 (Table 3). Furthermore, MRI revealed that RVEF was also decreased in ongoing AAS users compared with previous users and non-users, 48 (2) versus 55 (2) and 56 (2) %, P < 0.001. Structure Cardiac MRI-LGE did not show signs of focal myocardial fibrosis in any participants and postcontrast T1-mapping time did also not differ among the three groups suggesting the groups neither differed with respect to diffuse myocardial fibrosis (Table 3). Like echocardiography, cardiac MRI also demonstrated increased measures of LV mass in current abusers of AAS, P < 0.001 (Table 3). Further, current users of AAS featured concentric LV myocardial hypertrophy, with higher LV mass/EDV ratio, compared with former users of AAS and controls, 1.2

Comment [d3]: It,s near normal or mildly reduce LVEF

Comment [d4]: Hx of drug abus

Comment [d5]: Hx of drug abuse

Comment [d6]: Cardiac MRI findings are more precise than echo

(0.6) versus 1.0 (0.6) and 1.0 (0.4) g/mL, P < 0.05 (Table 3). Predictors of impaired cardiac systolic function and LV myocardial hypertrophy LV GLS We assessed if group-differences in LV GLS were independent of multivariate adjustment for study group, age, smoking history, use of other illicit drugs, weekly hours of resistance training, 24h systolic BP, heart rate, E/A ratio, LV mass/BSA, plasma MR-proANP, plasma SHBG and insulin resistance (Table 4). After multivariate adjustment, former AAS users still showed impaired LV GLS as compared with controls, group-difference: 1.4 (0.2 ; 2.6) %, P < 0.05; whereas difference in LV GLS between current AAS abusers and controls, no longer reached statistical significance (Table 4). Low plasma MR-proANP was strongly associated with impaired LV GLS in the

Comment [d7]: LVGLS should be come separately as LVEF , that both MRI and echo showed similar results.

4 - Milevski SV, Sawyer M, La Gerche A, Paratz E. Anabolic steroid misuse is an important reversible cause of cardiomyopathy: a case report. Eur Heart J Case Rep. 2022 Jul 2;6(7):ytac271. doi: 10.1093/ehjcr/ytac271. AF rhythm and cardioversion
In addition to GDMT
5 - Doleeb S, Kratz A, Salter M, Thohan V. Strong muscles, weak heart: testosterone-induced cardiomyopathy. ESC Heart Fail. 2019 Oct;6(5):1000-1004. doi: 10.1002/ehf2.12494.

6 - Gul U, Shahid M. Anabolic Steroid-induced Reversible Cardiomyopathy in a Young Non-athletic Female. J Coll Physicians Surg Pak. 2022 Feb;32(2):233-235. doi: 10.29271/jcpsp.2022.02.233.

7 - Baggish AL, Weiner RB, Kanayama G, Hudson JI, Lu MT, Hoffmann U, Pope HG Jr. Cardiovascular Toxicity of Illicit Anabolic-Androgenic Steroid Use. Circulation. 2017 May 23;135(21):1991-2002. doi: 10.1161/CIRCULATIONAHA.116.026945.

8 - Smit DL, Voogel AJ, den Heijer M, de Ronde W. Anabolic Androgenic Steroids Induce Reversible Left Ventricular Hypertrophy and Cardiac Dysfunction. Echocardiography Results of the HAARLEM Study. Front Reprod Health. 2021 Sep 1;3:732318. doi: 10.3389/frph.2021.732318.