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Patients who Seek Treatment for AAS Abuse in Sweden: Description of Characteristics, Substance Pattern and Mortality Rate

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Abstract

Objectives: Abuse of Anabolic Androgenic Steroids (AAS) has become a problem in Sweden. This study aims to describe retrospectively the characteristics of the first 102 treatment-seeking patients with primary AAS abuse in a specific endocrine clinic at a university hospital in Gothenburg, Sweden. The study parameters were sociodemographic status, medical and training history, mapping of the AAS abuse and use of other hormones and substances, and mortality rate.

Design and methods: During a ten-year period (1999-2009), 102 male patients were admitted to an endocrine clinic at the university hospital. All patients were asked about their former and current medical history and medication, sociodemographic status, including educational level, history of criminality and training history. Their AAS abuse was mapped, as was their use of other hormones and substances. A ten-year follow-up study investigated the mortality rate of the patients compared with the general male population.

Results: The mean age of the participating patients was 27.4 years (17-53 yrs.). The typical patient was co-habiting, had no children, had finished upper secondary school but had not gone to university, and almost half of them were employed. Almost half of them had an advanced criminal record. The patients reported a mean duration of AAS abuse of six years. The mean cumulative AAS dose was 200 grams, generally taken over ten consecutive weeks. They also had poly-substance abuse, including hormones (59%) and illicit substances (54%). An almost ten-fold premature mortality rate was noted among the patients, compared with the general population, with the main causes of death being cardiovascular disease and death secondary to the substance abuse.

Conclusion: This study is a dramatic illustration of the dangerous environment and lifestyle that are too often associated with AAS abuse. There appears to be an urgent need to establish specific treatment centers for this group of AAS abusers with other simultaneous substance abuse.

Keywords: Anabolic androgenic steroids; AAS; Hormone abuse; Resource centre; Mortality; Patient characteristics; Substance pattern; Poly-substance abuse

Introduction

Over the past decades, the illicit use of AAS has spread from elite athletes to the general population and is regarded today as a major health problem [1]. The Swedish Parliament has declared doping to be a societal problem, mainly due to the widespread use of AAS (Anabolic Androgenic Steroids) in gyms [2]. Data suggest that there are about 30000 (10000-100000) AAS abusers in Sweden today [3]. AAS account for most of the doping with hormones in gyms, but human growth hormone (hGH)/IGF-1 and insulin are also represented. A large proportion of individuals who use gyms also add other hormonal agents or performance-enhancing such as Growth Hormone-Releasing Hormone (GHRH)-stimulating peptides, thyroid hormones and ephedrine, to increase their performance [4].

The short-time somatic and psychiatric side effects of AAS are well described, including hyperlipidemia [5,6], liver problems [7], sexual dysfunction [8], extreme weight gain [9], atherosclerosis [10], hypertrophic cardiomyopathy [11,12], gynecomastia [13], ruptures of tendons and muscles [14], and premature alopecia [15], as well as severe mental problems, such as depression, psychosis and aggression [16]. Furthermore, an association between suicide and the use of AAS has been demonstrated [17-19]. Although the acute psychiatric effects are well described,

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less is known about whether former AAS abuse also leads to sustainable long-term effects on mental health [20].

Simultaneous use of alcohol and illicit substances, such as amphetamine, Gamma-hydroxybutyrate (GHB), cocaine, marijuana/cannabis and epinephrine, is also common and used as substitutes for AAS, especially when trying to discontinue the AAS abuse, temporarily or definitively [4]. This poly-substance abuse among gym-training individuals makes it hard to determine the impact of the AAS abuse as such, when discussing the long-term prognosis of AAS abuse in terms of morbidity and mortality.

Two studies have reported increased mortality, compared with the normal population, in elite athletes with suspected AAS abuse [19,21]. A controlled retrospective cohort study outside the elite sports scene observed a 20-fold increase in mortality in patients testing positively for AAS, in connection with receiving medical care for chest pain, depression or epilepsy, compared with patients with a negative AAS test [22].

The side effects of the other hormones used are also fairly well known. hGH has been used as a doping agent since the mid-80s and may mimic acromegaly symptoms when given in doping doses [23]. Short-acting insulin in doses of 30-50 units/day can lead to life-threatening hypoglycemia [24], as can doping with IGF-1, often together with strong headache [25]. Excessive doses of thyroid hormones, mainly used to induce weight loss via increased energy metabolism, may give rise to long-lasting catabolic situations [26]. The impact of this additional hormone abuse on the long-term prognosis is difficult to establish, as these hormone substances are often used in addition to the AAS, and thus during shorter periods.

The international literature shows that the use of AAS is positively associated with the use of alcohol, illicit substances and legal performance-enhancing substances [27], but the relationship between AAS and the use of tobacco and cannabis was found to be mixed and less clear. In 2013, a total of 46471 persons died of substance-induced causes in the United States; comprising 14.6% of the deaths in the total population when adjusted for age, a significant increase from 2012 by 5.8% [28]. The specific death register, Toxreg, in Sweden, designed to ascribe acute deaths related to narcotic substances over time, observed an increase in total deaths during the period 1994-2011,from 194 in 1994 to 487 in 2011, where heroin and amphetamine dominated both in 1994 (100 and 62, respectively) and in 2011(143 and 79, respectively)[29]. From 2006, there has been an increase in the legal prescription of opioids and methadone for the indications of pain relief and substitution therapy for heroin abuse, which may explain some of the mortality figures [30].

In 1999, a specific endocrine clinic was established for patients with former or current AAS abuse at a university hospital in Gothenburg, Sweden. The project was initiated as it was found that the number of AAS-abusing patients in the region increased steadily, and that the primary care system appeared to fail to offer these patients adequate treatment and care. The psychiatric clinic was directly associated with the project, as it was found that the patients often had psychiatric symptoms due to the hormone abuse itself, and/or to the simultaneous use of other illicit substances. Since the start, the endocrine clinic has further developed its primary treatment model and continuously gathered patient background data. A similar clinic for AAS patients was established in 2011 in Haarlem, the Netherlands, and the results presented indicate approximately 20000 AAS abusers in the country. The average patient was a 34-year old male whose abuse started at age 23 and presenting with poly-substance abuse. The majority of the patients showed typical AAS-induced side effects [31].

The aim of this retrospective study was to describe the characteristics and mortality of male patients with primary hormone abuse seeking treatment at the endocrine clinic at a university hospital in Gothenburg, Sweden. The study parameters, apart from mortality, were former and current medical history, including medication, sociodemographic status and illicit substance use.

Methods

Patients

Between 1999-10-04 and 2009-12-31, n=102 male patients, mean age 27.4 years (17-53), sought treatment for their AAS abuse at the endocrine clinic at a university hospital in Gothenburg, Sweden. The patients were referred to the endocrine clinic from general medical services such as general practitioners (GPs) or cardiology and psychiatric clinics. Patients who had contacted the endocrine clinic at their own initiative ("self-referrals") were also included. The specific reason for the referral to the clinic was noted for each patient.

Procedure

At the first visit, the first consecutive n=102 patients were asked exactly the same questions about their former and current medical history, including medication, and sociodemographic data, including educational level, criminal record, if any, and exercise history. The AAS abuse was investigated through questions concerning the age at the start of the AAS abuse and the number of years of AAS abuse (including information on the cumulative doses of each specific AAS agent and, if possible, the effects and side effects of the AAS agents). Use of other substances, including hormone substances, was also asked for. Furthermore, a somatic examination and laboratory tests, including routine and hormonal tests and heart function, were performed. On the basis of the results from the initial examination, the patients were offered follow-up visits at the clinic and/or consultations with, for example, psychiatrists, cardiologists, plastic or orthopedic surgeons, and, when needed, contact with the social services.

The pattern of the AAS abuse for each patient, up to the time of his first visit, was calculated on the basis of knowledge about each AAS agent, with regard to individual doses (mg/week), number of courses, the duration of courses (weeks), the number of courses per year and, finally, the number of years with AAS abuse. Thus, by multiplying these individual factors, the cumulative dose in mg/grams of each AAS agent at the time of the first visit was calculated. The pattern of other hormone doping

and substance abuse was also calculated through personal interviews. The mortality among the patients with at least one visit between 1999-10-04 and 2009-12-31 was retrieved from the National Bureau of Statistics and death certificates were obtained for deceased patients.

Statistics

The hazard functions of death in the general population as a function of age and calendar time were used. The functions were obtained from the National Bureau of Statistics and from the National Board of Health and Welfare (Sweden), publication series "Causes of Death". Thus, age and calendar time were taken into account. The start of the follow-up was the year when the patient was first admitted to the endocrine clinic. Using Poisson distributions, the difference between the observed and the expected numbers was tested and 95% confidence intervals (CI) of the hazard ratios (HR) were determined exactly. The expected number of total deaths—if the hazard function was equal to that of the general population—was calculated and compared with the observed number. The expected number was calculated as the sum of the products of the value of the hazard function of the general population and the total time of observation per year of follow-up. The difference between dead and living patients at follow-up concerning patient characteristics and substance doses was calculated using the SPSS statistics Independent Samples Kruskal-Wallis Test.

Ethical considerations: The study was approved by the Swedish Ethical Review Authority.

Results

Age

One hundred and two male patients were identified according to the inclusion criteria. The mean age of the patients at the time of admission to the endocrine clinic was 27.4 years (17-53) (SD±7.7) (Figure 1).

Reasons for clinic visit

The most common reasons for the patients to visit the clinic were an examination through self-referral; otherwise referral due to hypogonadism, gynecomastia, depression and subjective heart symptoms (Table 1).

Sociodemographics

The patients' sociodemographics are summarized in Table 2. About half of the patients were co-habiting/married or had a partner, but only about 25% had children. About 50% had finished upper secondary school, but only six patients had gone to university. Almost 50% had a permanent job, but more than one third were unemployed or on sick leave.

Medical history

One-third (33%) had experienced traffic accidents resulting in cerebral concussions/whiplash injuries and fractures (Table 3). Other accidents of a violent nature were also noted.

Criminal history

More than 40% had a criminal record, with assault and battery (including one case of attempted homicide), theft/robbery and drug dealing being the most frequent convictions (Table 4).

Training pattern

About two-thirds (68%) of the patients had performed team sports for some years in their youth, then, at the age of 17-18, they started training regularly in gyms. The main reasons for the gym training were the wish to develop a visible muscular appearance and to improve muscular strength. They started taking AAS agents at the age of 20 (Figure 2); i.e., after 2-3 years of regular training, and were motivated by the subjective feeling that their results from regular training had reached a plateau (Table 5).

AAS abuse

The substance pattern for different types of AAS agent and the doses and length of courses seem to be in line with previous reports for non-elite AAS users. At admission to the clinic, the mean duration of the AAS abuse was six years (0.05-30) and the mean patient age at the start of the AAS abuse was 20 years (14-33) (Table 6). About two-thirds declared that the abuse had stopped by the time of admission. The most frequent AAS abuse durations were 1.5-5 years (41%) and 5.5-10 years (24%). The mean estimated number of AAS courses was 14, with each course lasting ten weeks, on average. About 15 percent of the patients had a history of extended periods of AAS abuse for about three years (100 weeks). Thus, all patients admitted to the endocrine clinic

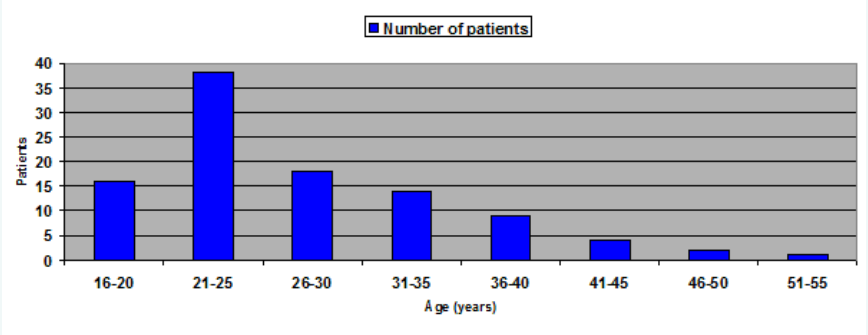

Figure 1 Patient's age at the time of the first visit to the endocrine clinic.

Table 1. The reasons, listed in order of frequency, for visits to the endocrine clinic.

Cause of general medical examination	Number of patients (n=102)
AAS – Examination and investigation	34
Hypogonadism	26
Gynecomastia	13
Depression	11
Subjective heart symptoms	6
Anxiety and sleeping disorders	4
Social problems	3
Alcohol or mixed substance abuse	2
Urinary tract symptoms	1
Hypothyroidism	1
Muscle strain	1

Table 2. Description of the patients' (n=102) personal data at the time of admission to the endocrine clinic.

Civil status	
Co-habiting, not married	32% (n=32)
Married	18% (n = 18)
Partner, living alone	5% (n = 5)
Living alone, no partner	33% (n = 33)
Living with parents, no partner	14% (n = 14)
Number of Children	
None	76% (n = 78)
One child	10% (n = 10)
Two children	8% (n = 8)
Three children	6% (n = 6)
Highest educational level	
Comprehensive school	(n = 24)
Upper secondary school	(n = 54)
Vocational training	(n = 11)
University	(n = 6)
Occupational status	
Student	12% (n = 13)
Employed	47% (n = 48)
Unemployed	20% (n = 21)
Sick leave	17% (n = 18)

had a history of previous or ongoing AAS abuse. Furthermore, almost three-fourths (73%) of the patients presented with poly-substance abuse, including other hormones/performance-enhancing substances (59%) and illicit substances (54%).

The mean cumulative AAS dose at admission was 200 grams. The most common cumulative doses were 25-100 grams (29%) and 100-300 grams (23%), together accounting for more than half of the patients. The proportions of the separate AAS agents and the simultaneous, additional hormone and poly-substance abuse, with regular use of each substance, are presented in Table 7. Methandrostenolone (79%), nandrolone decanoate (66%), sustanon (60%), stanozolol (59%), and testosterone enanthate (35%) were the most frequently used AAS agents and are the most common agents in the gym world (Table 7).

Additional hormone abuse

In addition to the AAS abuse, almost 60% (n=60) admitted to

Table 3: Description of the patients' medical history with regard to hereditary diseases and accidents at the time of admission to the endocrine clinic.

Hereditary history	
Cardiovascular disease	39% (n = 40)
Hormonal disease	21% (n = 21)
Substance abuse in family	32% (n = 33)
Injuries due to traffic or other accidents	
Concussion and whiplash	(n = 12)
Spinal injury	(n = 2)
Injury, not specified	(n = 3)
Fractures	(n = 14)
Gunshot wound to foot	(n = 1)
Fireworks injury to eye	(n = 1)
Assault and battery	(n = 1)
Other injuries	
Fractures	(n = 3)
Joints, muscles and tendons	(n = 7)
Lumbar spine injury	(n = 3)

Table 4: Description of the patients' criminal history at the time of admission to the endocrine clinic.

Overall criminality	
Number of patients convicted for:	43% (n = 44)
Violent crime	
Attempted homicide	(n = 1)
Assault and battery	(n = 20)
Robbery	(n = 3)
Possession of illegal weapon	(n = 1)
Crime involving property	
Theft and receiving	(n = 5)
Car theft	(n = 3)
Burglary	(n = 2)
Tax crime/economic crime	(n = 2)
Drug crime	
Narcotics	(n = 10)
Doping crime (and GHB)	(n = 7)
Traffic offence	
Drunk driving	(n = 2)
Speeding	(n = 1)

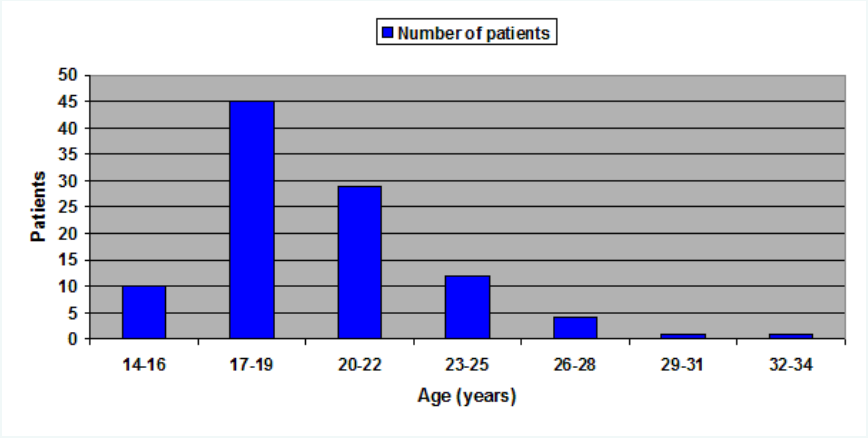

Figure 2 Patient's age at the start of the AAS abuse.

Table 5: Description of the patients' (n = 102) active training and the AAS abuse pattern at the time of admission to the endocrine clinic.

Age at start of gym training	17.5 yrs. (14-31)
Age at start of AAS use	20 yrs. (17-51)
Sports activity before start of gym training	
Team sports	68% (n = 69)
Combat sports	32% (n = 33)
Other individual sports	35% (n = 36)
Main reason for start of AAS use	
Further improve muscular strength	31% (n = 32)
Further develop muscular appearance	34% (n = 35%)
Training for body building competition	10% (n = 10)
Psychosocial reasons	24% (n = 24)
Stopped AAS abuse (verbal statement)	68% (n = 69)
Duration of AAS abuse (years)	6 yrs. (0.5-30)
Estimated duration of AAS abuse (weeks)	143 (2.5-840)
Estimated number of courses	14 (1-120)
Estimated length of course (weeks)	9.7 (2.5-16)
No. of extended periods of AAS abuse (n = 14)	2.8 (1-12)
Duration of extended periods in weeks (n = 14)	99 (20-260)
Mean total cumulative AAS dose (mg)	200 000 (900-2400000)

additional use of hormones in order to enhance their performance. Concerning the hormone abuse, hGH dominated by 35% (n=36), followed by insulin (19%) (n=19), and thyroid hormones (11%) (n=11). The daily hGH doses were about 2-6 units/day, 3-4 days per week, either in combination with AAS to inhibit a catabolic phase between the AAS courses, or administered alone to attain a lipolytic effect, preferably on abdominal fat. The subjective opinion about the performance-enhancing effect of GH ranged from "zero" to "excellent", the higher grading often being secondary to lipolysis. The frequent side effect of fluid retention was mostly reduced by taking diuretics.

Table 6. Mean duration of AAS abuse in the patients at the endocrine clinic.

Duration of AAS abuse (years)	Number of patients (n = 102)
<1	20
1-5	42
5-10	24
10-15	8
15-20	6
20-25	1
25-30	1

Additional substance abuse

The patients' medical history reveals that one third had substance abuse in the family. More than half of the patients (54%) admitted to additional use of other substances, of which amphetamine (36%), GHB (32%) and cocaine (24%) dominated. Regular smoking (34%) and alcohol use (regular social drinking) (44%) were also noted for a large number of patients (Table 7).

Mortality

Seven patients had died at the time of follow-up. The mean age at time of death was 28.8 years (23-47). The causes of death (ICD-10 diagnoses), according to death certificates, were heart disease (n=2), heroin poisoning (n=2), poisoning with other illicit substances(n=2) and unknown (n=1) (Table 8).There was an almost ten-fold increase (9.72) in the mortality rate in the patients compared with the control population, with seven (7) observed deaths, compared with the expected number of 0.72 (p=0.00002).The hazard ratio was 9.72 (95% CI: 3.90 – 20.04).

The substance abuse pattern in the deceased patients (n=7) versus living patients (n=95) at follow-up is illustrated in Table 9. In summary (not shown in the table), there was no significant difference between the two groups of patients with regard to their mean age of starting gym training (16.7 yrs.vs. 17.7; n.s.), start of AAS abuse (18.4 yrs.vs. 20.1; n.s.), mean duration of AAS

Table 7: Proportion and the doses of the separate AAS-agents and the contemporary mixed substance abuse.

AAS-agents	% (number)	Weekly dose (mg)	Total dose (mg)	Weeks (n)
Methandrostenolone	79% (n=81)	200 (35-550)	16 500	82
Nandrolone Decanoate	66% (n=67)	370 (50-1400)	50 100	135
Sustanon	60% (n=61)	540 (115-535)	38 300	71
Stanozolol (Winstrol)	59% (n=60)	205 (50-700)	15 800	78
Testosterone Enanthate (T Depot)	35% (n=36)	505 (250-1000)	66 300	131
Methenolene Acetate/Enanthate	34% (n=35)	380 (60-3335)	35 300	93
Trenbolone (Parabolan)	32% (n=33)	315 (40-1500)	29 900	95
Oxymetholone	28% (n=29)	390 (50-1040)	18 400	47
Testo Undecanoate	23% (n=23)	1320 (280-4200)	28 800	22
Testosterone Enanthate	22% (n=22)	715 (125-3500)	48 200	67
Omnadren	21% (n=21)	505 (125-1500)	23 000	46
Mixed substance abuse	*73% (n=74)*			
Other hormones and performance-enhancing substances	*59% (n=60)*			
GH	35% (n=36)			
Insulin	19% (n=19)			
Thyroid hormones	11% (n=11)			
IGF-1	7% (n=7)			
Ephedrine	31% (n=32)			
Clenbuterol	28% (n=29)			
Narcotics	*54% (n=55)*			
Amphetamine	36% (n=37)			
Gamma-hydroxybutyrate (GHB)	32% (n=33)			
Cocaine	24% (n=24)			
Marijuana/Cannabis	23% (n=23)			
Ecstasy	18% (n=18)			
Smoking-alcohol				
Smoking	34% (n=35)			
Alcohol use (social drinking)	44% (n=45)			

Table 8: Mortality according to death certificates (ICD-10 diagnosis code).

Age	1st cause of mortality	2nd cause of mortality
47	T404 Poisoning by Other synthetic narcotics (Pethidine)	
28	I258 Other forms of chronic ischaemic heart disease	T402 Poisoning by Other opioids (Codeine/Morphine)
		F102 Mental and behavioral disorders due to use of alcohol Dependence syndrome
27	I251 Atherosclerotic heart disease	F102 Mental and behavioral disorders due to use of alcohol Dependence syndrome
27	T438 Poisoning by Other psychotropic Substances, not elsewhere classified	T424 Poisoning by Benzodiazepines
26	T401 Poisoning by Heroine	R782 Finding of cocaine in blood
24	T401 Poisoning by Heroine	F102 Mental and behavioral disorders due to use of alcohol Dependence syndrome
23	R998 Unknown cause of mortality	

abuse (5.5 yrs.vs. 6.0; n.s.), or mean age at follow-up (25.4 yrs.vs. 27.5; n.s.).

The mean cumulative dose of all reported AAS substances was higher in the living patients compared with the deceased patients (206 ± 402 mg versus 106 ± 375 mg; n.s.), but did not differ significantly statistically. Also, the mean cumulative dose of the five most frequently used AAS substances did not differ between the two patient groups: methandrostenolone (26 297 mg vs. 17 291 mg; n.s.), nandrolone decanoate (14 240 mg vs. 73 213 mg; n.s.), sustanon (41 025 mg vs. 43 137 mg; n.s.), stanozolol (3480 mg vs. 19 667 mg; n.s.), and testosterone enanthate (54 167 mg vs. 79 235 mg; n.s.).

Contemporary use of hormone and other illicit substances is illustrated in Table 7, as absolute numbers and percentages for the

Table 9: Comparison between the diseased (n=7) and alive (n=95) patients.

At follow-up of the medians of total doses of the mostly used separate AAS-agents and the further hormonal/illicit substance abuse.

AAS-agents	Total dose dead (mg)	Total dose alive (mg)
All AAS-agents	106 375	206 402
Methandrostenolone	26297	17291
Nandrolone Decanoate	14240	73213
Sustanon	41025	43137
Stanozolol (Winstrol)	3485	19667
Testosterone Enanthate (Testoviron)	54167	79235
Methenolene Acetate/ Enanthate	2900	29269
Trenbolone (Parabolan)	1520	33276
Oxymetholone	3075	22574
Testo Undecanoate	9040	92789
Omnadren	3125	27971
AAS and hormonal/ illicit abuse	**Diseased (n;%)**	**Alive (n;%)**
AAS + GH	(n=3) 43%	(n=33) 35%
AAS + IGF-1	(n=0) 0%	(n=7) 7%)
AAS+Ínsulin	(n=0) 0%	(n=19) 20%
AAS+T3/T4	(n=0) 0%	(n=11) 12%
AAS+Clenbuterol	(n=3) 43%	(n=26) 27%)
AAS+Efedrin	(n=2) 29%	(n=30) 32%
AAS+Amphetamine	(n=4) 57%	(n=33) 35%
AAS+GHB	(n=6) 86%	(n=27) 28%
AAS+Ecstasy	(n=5) 71%	(n=13) 14%
AAS+hasch/marijuana/ cannabis	(n=3) 43%	(n=20) 21%
AAS+benzo + heroine + Rohypnol/LSD	(n=4) 57%	(n=8) 8%
AAS+regular ethyl use	(n=5) 71%	(n=40) 42%
AAS+smoker/ex.smoker	(n=3) 43%	(n=32) 34%

deseased and living patients, but due to difficulty of ascertaining the individual dose of each agent, no statistical effort was made to discover differences between the two groups. We do, however, notice that both groups admitted to contemporary GH abuse (42.9% vs. 34.7%), but none of the deceased patients had used IGF-1, insulin or thyroid hormones. Although not statistically tested, we noticed greater use of additional GHB, ecstasy and regular illicit substances among the deceased patients, who also had high alcohol consumption.

Discussion

This study describes the characteristics of the first 102 consecutive male, non-elite primary AAS abusers, who sought treatment for their abuse in a specific endocrine clinic at a university hospital in Gothenburg, Sweden. The typical patient was co-habiting, had no children, had finished upper secondary school but had not been to university, and only about half of them had a permanent job. Furthermore, a high proportion reported serious injuries due to accidents and almost half of them had an advanced criminal record.

The mean age of the patients was 20 years, and the mean duration of the AAS abuse was six years at admission to the clinic. The mean cumulative AAS dose was 200 grams, mostly taken in courses of ten consecutive weeks. Methandrostenolone, nandrolone decanoate, sustanon, stanozolol and testosterone enanthate dominated among the AAS agents used. Almost 60% admitted to additional use of hormones, most frequently hGH, followed by insulin and thyroid hormones. Regular use of other performance-enhancing agents, such as clenbuterol and ephedrine, was noted in about one third of the patients, and a good 50% admitted additional use of other substances.

Finally, an almost ten-fold premature mortality was noted among the patients, compared with the general population, after ten years of follow-up; the main causes of death being cardiovascular disease and death secondary to the use of narcotic substances. Other than that, no difference was noted between the dead and living patients with regard to the duration and cumulative dose of the AAS abuse. The results from this study are a stark illustration of the dangerous environment and lifestyle that are too often associated with gym training and simultaneous AAS abuse.

Through very strict personal interviews, where all the patients were asked exactly the same questions, we have achieved reliable figures concerning the substance pattern of the patients, including the cumulative dose of each specific hormone substance. However, the nature and doses of the other illicit substances may not be that specific compared with the AAS and other hormone substances, mostly due to the difficulty of presenting the illicit substances in grams per day.

The most common reason for the patients to visit the endocrine clinic was an examination through self-referral, indicating the importance of the clinic to answer the patients' questions and fear about the AAS abuse and its possible complications. This informal way to contact the clinic seems to be important in order to reach new patients. Otherwise, not surprisingly, the reasons through regular referral were hypogonadism, gynecomastia, depression and subjective heart symptoms; all known side effects of long-term AAS abuse.

The gross mean characteristics of the typical patient seeking help for his AAS abuse thus reveal a patient with a sometimes heavy social burden, including family substance use habits, educational level and job situation, incidence of serious accidents and criminal record; factors which, taken together, may explain many of his problems. The connection with this inferior degree of socialization, including criminal records and poly-substance abuse, has been observed in previous studies, and is important to recognize in order to understand and find proper ways to end the AAS abuse [32-34]. The role of psychiatric teams and social workers in this work is of the utmost importance. We have no exact figures concerning the incidence of domestic violence,

but we are fully aware of the problem, as many patients came to the first visit with their partner, when the problem was well described, and the partner threatened to leave the patient if no change in the situation was forthcoming. This illustrates clearly one of the main factors for a successful result in this type of clinic; that is, with the cessation of AAS use the patient and his partner will achieve improvement in their social lives.

The observed poly-substance situation, in addition to the AAS abuse, including both other hormones and other illegal stimulants, is a well-known phenomenon among non-elite AAS users [35,36].This poly-substance use was also described in another Swedish study of 34 AAS users in gyms, where more than half of the patients were using substances of abuse and also taking various other pharmaceuticals [37]. Almost half of those patients also used hGH, and were drinking alcohol to a hazardous or harmful extent. Due to local and national factors concerning the accessibility, cost and habits of using specific hormone or illicit substances, there may be differences in the poly-substance pattern in different studies. However, we believe that the pattern described in the present study is rather typical of Swedish non-elite AAS users. This poly-substance situation creates general treatment difficulties during both the active AAS abuse periods, but also during the following AAS-free period, where the non-AAS agents may replace the previous, subjectively positive, AAS effects. Thus, amphetamine misuse following cessation of long-term AAS use is unfortunately seen too often, although other contemporary illicit drug abuse, including amphetamine use, also occurs in situations of no AAS-free periods [37].

Our study reveals a rather uniform pattern describing the patients' training history and its relation to the start of AAS use. Typically, the patient presents a history of interest in all sports, often team sports, which is replaced by gym training at the age of 15-18 years. The gym training is motivated by a wish to improve body appearance or simply muscular power, in some cases, from a subjectively lean or obese body composition. The AAS use starts, on average, after 3-4 years of clean gym training; that is, at 20 years of age, when, according to the patient, the training results have reached a level where no further improvement seems possible, a situation these patients do not accept. In some, the training had given rise to expectations of reaching the optimum body composition results, not seldom influenced by well-known bodybuilders. Others started their AAS use after pressure from gym mates, who had noted subjectively good results with AAS. Still others felt curious about the AAS agents, and decided to test one or two courses.

The substance pattern for different types of AAS agents and the doses and length of courses seem to be in line with previous reports on non-elite AAS users [34]. The mean cumulative AAS dose among the patients was 200 grams, mainly taken during ten consecutive weeks. A subgroup of the patients showed a mean AAS duration of about 100 weeks. However, an earlier report from the Netherlands showed that in about 50% of illegally obtained AAS, the contents do not match the description on the label, thus leading to uncertainty about the doses and, consequently, their correlation with side effects [38].

A mean duration of six years of AAS abuse was noted among the patients in the present study. The reasons for giving up the AAS use range from intolerable side effects, including fear of future infertility or heart disease, to pressure from girlfriends and relatives, and social consequences including legal consequences, as the use of AAS is illegal in Sweden (personal communication, data not shown). However, some patients present with 20-30 years of AAS abuse, with explanations such as dependency on the substance, and that training with simultaneous AAS abuse has created a specific positive character for the patient, with admiration from his local and distant friends, and the impression "of being somebody"; a situation that the patient does not automatically want to give up.

The short-time somatic and psychiatric side effects of AAS are fairly well described, as we have presented in the introduction part of the paper [8,11,12,16]. In addition, it appears that about one-third of the patients develop an AAS dependency situation [39]. Also, the negative effects of AAS on the cardiovascular system need some special comments. These side effects include a tendency towards myocardial hypertrophy and alterations of diastolic function and ventricular relaxation and, most likely, subclinically compromised left ventricular contractile function; changes that occur after 3-4 months of AAS abuse [40]. AAS also induce a mild but transient increase in blood pressure, an enhanced pro-thrombotic state and an increased risk of potentially life-threatening arrhythmia [40]. AAS produce negative alterations of the lipid metabolism, with mainly a decrease in HDL and an increase in LDL concentrations [41].AAS also often cause secondary polyglobulism, at times leading to extreme values of hemoglobin and hematocrits, with a resulting need for urgent venesection [42].Taken together, these data strongly suggest an increased risk of cardiovascular disease among users of AAS, but a spontaneous reversion of these harmful parameters may occur after cessation of the AAS, and patients must be informed about this [43].

About 1/3 of the patients reported use of clenbuterol, ephedrine and amphetamine. Clenbuterol is a beta-2 agonist with the same effects as a general stimulant and thermogenic substance. It is used in the gyms mainly for its anabolic side effect. Furthermore, it increases aerobic capacity, central nervous system stimulation, blood pressure and oxygen transportation. Moreover, body fat is metabolized due to an increased basal metabolic rate (BMR) [44]. Ephedrine and amphetamine may also have adrenergic side effects in high doses on both the cardiovascular system and the CNS. The ephedrine cardiac side effects include hypertension, arrhythmias and myocardial infarction, with an obvious risk of acute death. The CNS symptoms include tremor, anxiety and psychosis [45].The corresponding amphetamine response comprises tachycardia, hypertension, hyperthermia and the well-known acute euphoria, relief of fatigue and increased self-confidence, and finally aggressive behavior and psychosis [46].

The number of long-term studies concerning mortality and AAS abuse outside the elite sporting world is still limited. A Swedish study, where patients testing positively for AAS in

connection with receiving medical care, showed an increased mortality rate of about 20 times compared with the normal population [22].There are very few studies from the world of elite sports dealing with the long-term risks of AAS doping. A Finnish study including 62 male elite power-lifters showed a four-fold mortality increase during a 12-year follow-up period in the lifters compared with controls, with suicide and cardiovascular diseases dominating among the causes of death [21]. A similar follow-up study of about 1100 Swedish male elite athletes in power sports, active in 1960-1979, showed a 40% increase in total mortality during and 10-15 years after the end of their career [19]. In both studies, former AAS abuse was considered a plausible cause of the premature mortality. To our knowledge, this is the first study with long-term mortality follow-up of non-elite gym-training men, all with a history of past or current AAS abuse, but also a history of additional mixed substance abuse.

There were no differences between the seven dead patients and the remaining 95 patients concerning the age at start of AAS use and the duration of the abuse. Also, the cumulative AAS doses did not differ between the dead and the living patients. There was, in fact, no use of IGF-1, insulin and thyroid hormones among the dead patients. Although not significant, the doses of illicit substances, such as amphetamine, GHB and ecstasy, as well as their consumption of alcohol, seemed high among the dead patients. Taken together, this indicates that these patients represent a specific group in the gyms, characterized by a sort of omnipotent and thoughtless character, resulting in a less strict training schedule and including addition of illicit substances to their AAS use. The thoughtless character typically demonstrates an inability to understand risks before they occur; that is, they often consider themselves to be continent men although they simultaneously use harmful drugs, without understanding the risks involved. This is contrast to the other group, which performs their training in a more serious way, primarily to achieve an increase in muscular appearance, and therefore avoid deleterious illicit substances. These two different groups are easily recognized when dealing with AAS patients in the specific clinical centers, and the less seriously controlled group often seems to be in greater need of specific psychiatric help. Furthermore, there is a third well-characterized group, however not noticed among our patients, which uses AAS primarily to develop an uncaring mind for criminal purposes, without a specific desire to enhance their physical strength.

Although a small number of deaths in absolute terms, the mortality pattern shows a predominance of death causes from poisoning with illicit substances (n=4) and cardiovascular disease (n=2). Furthermore, the complexity is underscored by the fact that the two patients dying from atherosclerosis also had secondary death causes of alcoholism and opioid dependence, respectively. Although opioids usually cause premature deaths due to overdose, the poly-substance pattern of AAS abuse and other illicit substances may in itself cause interactive situations, where the known side effects of AAS and illicit substances are multiplied, which explains the increased mortality.

The mean duration of the AAS abuse was six years, although several patients had used AAS for 10-20 years, apparently without any side effects, suggesting a possible individual variation concerning side effects and probably also concerning positive AAS effects. This individual variation observed among the patients may be explained by changes at receptor level, and by differences in the metabolism of the individual AAS agents [47]. The small number of deaths, and short exposure time for those patients who died early, made it difficult to make relevant correlations between the cumulative AAS doses and the risk of death. However, from our clinical experience, we may speculate about a possible threshold concerning the AAS regimen producing side effects, and where additional doses do not seem to have any further deleterious effect.

The effect of the other hormone abuse on mortality is more difficult to ascertain, especially as only hGH, but not insulin, IGF-1 or thyroid hormones, was taken by the patients who died. The impact of the corresponding illicit substances on mortality is clearly illustrated when studying the death certificates. Thus, four patients had substance poisoning as the first cause of mortality: two from heroin, one from pethidine and one from a non-identified substance. Furthermore, the two patients who died from heart disease both had illicit substances as the second cause of mortality: opioids and alcoholism, respectively. At admission to the clinic, about half of the patients admitted to other substance abuse, where amphetamine, cocaine and alcohol dominated, although the figures for heroin may be underreported. The illicit substance abuse among the gym patients on regular AAS use is a major problem that we have been aware of when treating the patients in the endocrine clinic. Without the assistance of the psychiatric services connected to our clinic, the mortality figures for depression, psychosis and illicit substance abuse would have been even higher. However, one major problem for the specific clinic is the lost patients, meaning patients missing return visits, despite repeated calls. It is essential that AAS clinics include staff and actions that can handle the bad/threatening social situation often connected with the patients, in addition to dealing with the misuse of AAS and the illicit substances.

This ten-year follow-up study describes the characteristics of 102 male, non-elite primary AAS abusers, who seek help for their abuse in a specific endocrine clinic in Gothenburg, Sweden. Almost 60% admitted to additional use of hormones, most frequently hGH, followed by insulin and thyroid hormones. Regular use of other performance-increasing agents, such as clenbuterol and ephedrine, was noted in about one-third of the patients, and a good half of the patients admitted to additional use of other substances. This poly-substance situation must be considered when trying to explain the almost ten-fold premature mortality rate among the patients. The results from this study are a stark illustration of the dangerous environment and lifestyle that are too often associated with gym training and contemporary AAS abuse. There seems to be an urgent need to establish specific treatment centers for this group of AAS misusers with simultaneous other substance misuse.

Declaration of interests

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contributions

Study concept and design: E Edin, C Ehrnborg, S Ljungdahl and T Rosén. Acquisition of data: S Ljungdahl and T Rosén. Analysis and interpretation of data: C Ehrnborg, S Ljungdahl, and T Rosén. Drafting of the manuscript: S Ljungdahl. Critical revision of the manuscript for important intellectual content and final approval: C Ehrnborg, B Eriksson, C Fahlke, A-S Lindqvist, S Ljungdahl, T Moberg and T Rosén.

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