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DOI 10.2478/afepuc-2022-0012.

HEART DISEASE AFTER COVID: EXACERBATED FUTURE HEALTH RISKS ALIGNED TO PREVIOUS AND EXISTING AAS/ANDROGEN USE

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Summary: In this commentary/short communication we build upon our existing research and viewpoints related to the deleterious effects that AAS/Androgen use has, and the growing body of work and case studies/reports that identify the substantially increased risks that AAS/Androgen use presents to those who have (or have had) COVID-19. We position this commentary/short communication then, as one that builds on our prior calls for public health policy to be in part framed by, or at least to recognise the risks, of AAS/Androgen use. This is of particular contemporary importance now that COVID-19 is endemic, and we report on how long COVID-19 (Post COVID-19 syndrome) can present a wide range of lasting cardiovascular problems, a particular issue given that AAS/Androgen use may well exacerbate future health risks aligned to COVID-19.

Key words: Post COVID-19 Syndrome; Myocardial Dysfunction; Public Health Policy, Anabolic-Androgenic Steroids (AAS) /Androgens

Introduction

The announcement of COVID-19 as a novel coronavirus on 1 December 2020 (WHO 2021) has led to more than 6,522,600 deaths worldwide, reported to the World Health Organisation [WHO] (WHO, 2022), by end of September 2022. This is despite significant attempts to reduce transmission through public health measures such as lockdowns, the advancement and availability of various medicinal treatments (i.e. antibody and antiviral

medicine), and the creation and establishment of highly effective vaccinations. The last of these, effected through comprehensive governmental vaccination programmes that have positioned immunization as a key component of health care, has significantly mitigated the spread and severity of the disease, and reduced deaths attributable to COVID-19 to what are now universally considered manageable and acceptable levels (for instance, more comparable with excess deaths attributable to influenza).

In England and Wales, for instance, whilst the death toll between 13 March 2020 and 1 April 2022 for COVID-19 and influenza (and pneumonia) were 148,606 and 35,007 respectively (where they were identified as the underlying cause of death, not where it was recorded as a contributory factor - Office for National Statistics [ONS] 2022a), and indeed, reported deaths from COVID-19 reached peaks of 1,461 on 8 April 2020 and 1,490 on 19 January 2021, these higher peaks were not sustained. Lockdowns, vaccines, pharmaceutical control measures, and novel medicinal treatment significantly mitigated transmission and infection rates, and by 16 September 2022 COVID-19 deaths were down to 42 per day (coronavirus.data.gov.uk 2022). These numbers are roughly equitable to the aforementioned figure of 35,007 deaths attributable to influenza between 13 March 2020 and 1 April 2022, which equates to approximately 50 deaths a day.

With the key strategy of ensuring ICU occupancy thresholds did not exceed capacity (ONS 2022b), and the fact that the more telling pressures of the worldwide public health emergency have abated (subsequent to the establishment of an effective vaccination programme), the manner in which COVID-19 has affected public services (and the economic implications) are now front and centre of political expediency and COVID-19 scenario modelling and planning. Indeed, as various governments tentatively move to inhabit the new societal terrain of an endemic virus, questions arise as to how proposed approaches address the roles and responsibilities within contemporary emergency and contingencies preparation. Futureproofing for novel viruses, or new variants, and adhering to the views of biomedical scientists highlights the need for working alliances between epidemiologists, economists, and behavioural scientists, and the need for governments to accede some power whilst drawing up robust intervention and prevention methods. It is in the spirit of the principles of prevention, that we present this short commentary to both update some of the latest, confirmatory research related to our previous viewpoints, and continue to espouse public health discourse related to the novel and nuanced problematics related to AAS/Androgen use and COVID-19.

AAS/Androgens are synthetic drugs derived from testosterone (Saudan et al. 2006). These drugs are prescribed for conditions such as hypogonadism as well as chronic

wasting conditions through increased appetite and stimulating muscle growth. However, the adverse chronic health effects they elicit can include, but are not exhaustive to, multiorgan damage (Samaha et. al. 2008), negative cardiac effects (Ismail et al. 2012), increases in mortality risk for users (Pärssinen et al. 2000), as well as a plethora mental health issues (van Amsterdam et al. 2010). These kinds of deleterious effects are also well recognised in terms of scale (significantly higher) when occurring within unsupervised, non-medically supported (illicit), recreational contexts (Sagoe et al. 2014). The work of Wood (2008) and Seear et al. (2015), for instance, illustrate the ways in which addiction and hepatitis risk from injections are areas of particular concern when it comes to unsupervised AAS/Androgen use in the general population.

Our previous ethical considerations and principles of research and commentary have, admittedly, taken on a polemical tone. A tone, however, that has been focused on how AAS/Androgen elicits the aforementioned well-documented, negative health implications, yet has also highlighted more novel discourse related to the identification of possible negative links between recreational AAS/Androgen use and what was (then) fast published data related to compromised immune responses through COVID-19, oftentimes due to hyperinflammatory responses (Crisp & Sims 2020b/2021). Indeed, our overarching aim throughout our papers related to this area has been to strongly recommend that public health discourse and mandates help shift the reality of how recreational AAS/Androgen users make agentic decisions, to one that educates potential users to the emerging empirical evidence that demonstrates how AAS/Androgen use can exacerbate COVID-19 symptoms and negative responses (Crisp & Sims 2020a/2020b/2021).

Moreover, our last paper outlined the pressing issue of how AAS/Androgen use increased post pandemic and lockdowns, thus potentially magnifying future health issues (Crisp & Sims 2022). This short communication acts as a timely update then to this last paper, in that the fast-response literature has started to repeatedly support some of our more suppositional ideas, as well as highlight how - without proper public health discourse related to AAS/Androgen use as another risk factor - some who may present as outwardly healthy may be partially hidden as at risk of heart issues related to COVID-19.

Previous research has demonstrated that AAS/Androgen use can exacerbate respiratory distress for those suffering from pneumonia (e.g. Mayer et al. 2016; Bhanot et al. 2016). Moreover, we surmised the negative effects that AAS/Androgen use could play in compromising immune responses (Crisp & Sims 2020b), something particularly germane in COVID-19 reactions. Related to this, Cadegiani et al. (2021a) outlined the severe response to

COVID-19 suffered by an otherwise healthy 28-year-old AAS/Androgen user, and posited that the mechanisms that fight COVID-19 are impacted by the misuse of AAS/Androgen. Furthermore, Althobaiti et al. (2022) in a study of 520 gym-attending participants, found within this sample that current users of AAS/Androgens were nearly five times more likely to contract COVID-19 than non-users. Indeed, successful early antiandrogen therapy has been shown to be effective in reducing inflammatory responses and other adverse effects caused by COVID-19 (Cadegiani et al. 2021b), thus demonstrating the harmful effects that AAS/Androgens possess.

Whilst there is, admittedly, a more limited amount of direct evidence available that demonstrates case studies of young adults with no previous health concerns suffering severe COVID-19 responses, and where AAS/Androgen use is highlighted as a credible potential link to COVID-19 disease severity because of AAS/Androgen use, more is coming to light. For instance, Al-Hajjaj et al.'s (2022) second case report of a 32-year-old AAS/Androgen user with severe COVID-19 symptoms attributable to AAS/Androgen use and treated with antiandrogen therapy. So whilst is clearly recognised that AAS/Androgen plays a role in immunosuppression, hyperinflammation, and acute respiratory distress, it has also become increasingly acknowledged that these reactions can further complicate COVID-19 infection (Crisp & Sims 2021).

In addition, we now contemplate how long COVID-19 (or post COVID-19 syndrome) may very well change approaches to cardiac event monitoring (NHS 2022). This is particularly in the manner in which specific challenges, issues, and literature outlines how those that have had COVID-19 have increased risk of heart attack, strokes, or other cardiovascular conditions. Indeed, and as Sidik (2022) outlines, it is generally agreed that COVID-19 and long COVID-19 can present a wide range of lasting problems. cardiovascular problems and the heart and circulatory system can be permanently damaged, but also other organ damage (i. e. lungs, brain). The significant issue here then – now that the consensus of research demonstrates possible lifelong risk for heart attacks and other cardiac events following COVID-19 - is gaining an understanding of which at risk groups who have, or had, long COVID-19 can be identified.

Accurate estimation of the prevalence of ASS/Androgen use within the UK population is difficult given the proscribed nature of this behaviour. Despite this, figures from the ONS show an average of 0.8 % of the population of England and Wales aged 16 - 59 years reported illicit ASS/Androgen lifetime use (ONS 2020). Of those engaging in ASS/Androgen use, it is highly likely that is not restricted to a single episode when we take into account that a particularly salient feature of recreational ASS/Androgen use is extended cycling practices (Cohen et al. 2007). Given, therefore, the protracted and insidious nature of many risk factors

that lead to additional mortality and morbidity subsequent to COVID-19 infection, as well as the potential contribution AAS/Androgen use possesses for the lifetime incidence of these risk factors, the likelihood of combinatoric health detriment requires careful screening and planning within health services.

At first glance identifying at risk groups this may well seem simple enough, as existing public health strategies and understanding have long estimated prevalence of those at risk due to morbidity, such as those with diabetes, chronic obstructive pulmonary disease, pneumonia, or cystic fibrosis, or those exhibiting risk behaviours, such as smoking, low physical activity, obesity. However, in line with our previous research and stances related to AAS/Androgens (Crisp & Sims 2021/2022), the fact that AAS/Androgen use is associated with myocardial dysfunction and other cardiac events (Baggish et al. 2017), and the emerging case studies that show otherwise healthy adults who use AAS/Androgens suffering severe COVID-19 symptoms (Cadegiani et al. 2021a; Al-Hajjaj et al. 2022), then if someone takes AAS/Androgens or have done for a period of time, it could well present significant problems at some point in the future. The issue here then is that AAS/Androgens are thus another risk factor, yet one that is partially hidden as many who use them present as outwardly healthy.

Given that medical literature now explicitly outlines the emerging dangers of long COVID-19 for at risk groups, in particular those who have had previous heart issues or who indulge in practices such as smoking and AAS/Androgen use that specifically damages heart tissue and function, then we posit that public health strategies (and discourse) that monitor and mitigate heart risk factors for those who suffer long COVID-19 must also understand and outline how AAS/Androgen use can contribute to severe long COVID-19 responses. We believe, given the potential lifelong risk factors, that this necessitates health work practice and plans that specifically challenges and/or supports AAS/Androgen use in terms of preventative knowledge and education, and that this information must be made part of policy and direction for both users and health practitioners

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