



Editorial

The Cardiovascular Effects of Testosterone as Gender Affirming Treatment for Adolescents: Areas for Future Investigation



The health care of gender-diverse adolescents remains an ever-growing and evolving field composed of professionals and researchers working to improve the quality and delivery of care to patients. The article by Kean et al. featured in this issue of JAH was created by an interdisciplinary team of pediatric cardiologists, adolescent medicine specialists, and endocrinologists with a common goal. They have written a narrative highlighting the limitations of the existing literature and clinical guidelines on the care of gender-diverse youth using testosterone for gender affirming hormone therapy (GAHT) in regard to the cardiovascular effects of the medication [1]. The undertaking was completed with the hopes of inspiring the generation of future studies to meet these needs. The authors explain that although literature exists on the cardiovascular effects of testosterone on cisgender individuals, studies on the long-term effects of testosterone use in gender-diverse adolescents are lacking. For those prescribing testosterone for gender-diverse adolescents, providing appropriate counseling is paramount. Well-informed counseling empowers both providers and patients with the ability to monitor for early signs of adverse effects and potentially mitigate or avoid them entirely. As part of this call for action, the authors provide a veritable road map for future directions of research. Key areas highlighted include the requirements for data around the effects of testosterone in youth who have already completed a puberty modulated by estrogen, additional studies on adolescents starting testosterone, and more robust information to inform anticipatory counseling and preventative care.

Kean et al. initiate the narrative with a historical perspective of testosterone use, illustrating the changes in use and guidelines over time as additional data have been gathered [1]. Furthermore, a conceptual framework is established regarding testosterone use and cardiovascular health. The contributions of the interdisciplinary team involved in the research provide a well-rounded perspective on the interactions described, which is very appropriate considering that the care of gender-diverse adolescents is often an interdisciplinary effort. Within the framework, the cardiovascular endocrinology of testosterone is explored, describing what is known about the effects of testosterone on cells and

tissues. The next piece of the framework describes the effects of testosterone on cardiovascular physiology, while indicating the need for research into the risks of acquired heart disease in individuals using testosterone for GAHT. There, the subsection on cardiac electrophysiology illustrates the hormonal effects on electrocardiogram findings, which have not yet been studied in gender-diverse youth on GAHT. Additional attention is paid to the effects of stress and anxiety on cardiac symptoms. This article goes on to discuss vascular pathology, where the future risks of atherosclerosis have not been explored yet in youth on testosterone. The final segment in the section on physiology is particularly timely, as it addresses the knowledge gaps around exercise physiology in a time when many states have considered or passed legislation regarding the participation of transgender athletes in sports. As there are no significant normative data on the fitness goals and capabilities of individuals on GAHT, it is difficult to provide evidence-based management or counseling on the topic.

Before its conclusion, the article discusses the potential psychological and behavioral influences on cardiovascular risk that can occur in individuals utilizing testosterone for GAHT. As the article indicates, we must also consider the other factors at play that may increase cardiovascular risk, including the stressors that may be experienced in an unsupportive environment. Stress/discrimination and anxiety are highlighted as gender-diverse individuals may experience discrimination, negative family dynamics, and even life-threatening violence [2]. The use of GAHT has been associated with decreases in depression, stress or cortisol awakening, anxiety, dysphoria, psychiatric stress, and psychological concerns [3–9]. The cardiac effects of eating disorders are discussed in this section, as testosterone has also been shown to aid in decreasing body dissatisfaction and uneasiness, along with helping decrease eating disorder symptoms [10–12]. Improved sense of well-being and quality of life are also reported [6,13]. Tobacco use, as a risk factor for cardiovascular disease and its prevalence among gender-diverse individuals, is discussed along with fascinating insight as to why it may be continued [1].

The authors conclude with clearly identified gaps that exist in the known literature, sending out a call for new research,

See Related Article on p.896

especially considering that the current resources may not apply to adolescents starting testosterone [1]. To provide well-rounded counseling and anticipatory guidance, additional details and long-term outcomes are needed. Kean et al. leave readers with excellent advice for the time being: to treat the current organs present in a patient, while recalling the known effects of treatment on them.

Considering the existing research, it is clear that the benefits of GAHT for patients experiencing gender dysphoria outweigh the potential risks. Getahun et al. demonstrated that testosterone can be used for GAHT in a safe and effective manner [14]. A review completed by Connelly et al. illustrated the paucity of studies showing an increased risk of cardiovascular or cerebrovascular disease, even with elevations in blood pressure and dyslipidemia, in gender-diverse individuals on testosterone compared with cisgender men [15]. The diversity of adolescents utilizing GAHT must also be considered. For one, individuals taking testosterone may vary widely in terms of dosing, as it may differ based on age, health, needs, or preference, among others. Some adolescents may opt for lower dosing (e.g., microdosing to present as nonbinary), to stop use after the presence of permanent effects, or take breaks from testosterone use (e.g., desiring pregnancy). Very little is known about these groups, and they should not be excluded from future endeavors. Family history of cardiovascular risk will also likely be a contributor of risk.

One must also think of the benefits that improved information in this area could provide in the realm of expansion of services, as a lack of knowledge may be cited as a reason why providers do not prescribe GAHT [16]. With all considered, we wish to improve the quality of counseling and clinical management but to not increase the barriers to what may be a lifesaving treatment for individuals who may have already overcome a lifetime of obstacles and challenges.

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