Lack of association of exogenous testosterone administration with exacerbation of preexisting hidradenitis suppurativa

To the Editor: Hidradenitis suppurativa (HS) is a painful inflammatory skin condition disproportionately affecting women.[1] Previous studies have suggested a link between androgens and HS[2] and androgen-modulating therapies are commonly used to treat mild and moderate HS.[3] There are only 3 published cases of exogenous testosterone (ET) in association with either new-onset HS or exacerbation of existing HS.[4,5] Here, we conduct a cross-sectional evaluation of the risk of HS exacerbation within 6 months of initiating ET therapy in patients with preexisting HS diagnosis.

International Classification of Disease, *Tenth Revision* codes were used to identify all patients with a dermatology-verified diagnosis of HS and prescription for ET in the Mass General Brigham Research Patient Data Registry from November 2016 to November 2022. Through individual chart review, history of prior HS exacerbation (defined as HS-related emergency department visits or hospitalizations, dermatologic documentation, or treatment escalation) was collected for all patients in the 6 months prior to initiating ET. HS exacerbation in the setting of ET therapy was defined as exacerbation occurring within the first 6 months of treatment. Significance was calculated using Fisher's exact testing.

Thirty-one patients with a mean (SD) age of 48.45 (14.3) years met the inclusion criteria for this study (Table I). A sample size of 40 subjects was required to achieve power based on standard assumptions. Seven (22.6%) patients, the majority of whom were non-Hispanic White ($n = 5$, 71.4%) cisgender men ($n = 6$, 85.7%) with Hurley stage I or II disease, experienced at least 1 disease exacerbation in the 6 months prior to ET therapy (Fig 1). After initiating ET, 2 (28.6%) of the 7 continued to have HS exacerbations, while 5 (71.4%) remained stable. Of the 24 patients that did not experience HS exacerbation in the 6 months prior to ET, 2 patients (8.3%) experienced worsening HS in the 6 months after initiating ET. There was no significant association between ET use and HS disease exacerbation ($P = .51$). Subgroup analysis of the 24 cis-gendered men prescribed ET for hypogonadism demonstrated similar lack of significance ($P = .2$) Only 2 patients were on testosterone-modifying medications (finasteride, dutasteride, or spironolactone). Clinical characteristics of the patients who experienced exacerbations of their HS can be found in the Supplementary Material, available via Mendeley at https://data.mendeley.com/datasets/3fk4nvthmw/1.

In this study, we found no statistically significant association between ET use and exacerbation of a patient's baseline HS. In general, patients without previous history of HS exacerbation in the 6 months prior to ET therapy remained exacerbation-free in the first 6 months post-ET therapy. Moreover, there was no clear connection between patients who had disease exacerbations prior to ET and the few that who had them after ET.

The findings of this study highlight the need for further investigation into the role of androgens in HS pathophysiology including additional translational work to elaborate the mechanism through which antiandrogen medications, including spironolactone, contraceptives, and finasteride, act to treat HS.[3]

There are several limitations to this study. Although the timeframe of this study represents 6 years of patient data at a major academic center, the small sample size and cross-sectional study design limit our ability to draw causal conclusions. Power was not achieved despite wide timeline and large initial data set. The primary involvement of cis-gendered male subjects makes generalizations across sexes challenging. Doses of ET differed across individual and testosterone type as well. There is likely sampling bias in our data as patients with severe HS may have never been prescribed testosterone for fear of disease exacerbation. Future large-scale prospective studies are needed to further elucidate the relationship between exacerbation of preexisting HS and use of ET therapy.

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Table I. Participant demographics and clinical characteristics of patients with hidradenitis suppurativa before initiation of exogenous testosterone

Patient characteristics *n* (%)	Patients with HS exacerbation(s) before initiating ET (*N* = 7)	Patients without HS exacerbation(s) before initiating ET (*N* = 24)	Overal (*N* = 31)
Age, y (mean [SD])	47 (13.5)	49 [14.8]	48.5 [14.3]
Sex			
Cisgender man	6 (85.7%)	19 (79.2%)	25 (80.7%)
Cisgender woman	0 (0%)	3 (12.5%)	3 (9.6%)
Transgender man	0 (0%)	2 (8.33%)	2 (6.45%)
Transgender woman	1 (14.3%)	0 (0%)	1 (3.2%)
Race			
White	5 (71.4%)	21 (87.5%)	26 (83.9%)
Black	0 (0%)	1 (4.2%)	1 (3.2%)
Asian	0 (0%)	1 (4.2%)	1 (3.2%)
More than 1 race	0 (0%)	1 (4.2%)	1 (3.2%)
Not disclosed	2 (28.6%)	0 (0%)	2 (6.5%)
Ethnicity			
Hispanic	2 (28.6%)	2 (8.3%)	4 (12.9%)
Non-Hispanic	5 (71.4%)	19 (79.2%)	24 (77.4%)
Unknown	0 (0%)	3 (12.5%)	3 (9.7%)
Duration of hidradenitis suppurativa, y (mean [SD])	9.71 [5.9]	10.67 [23.1]	10.45 [20.4]
Hurley stage prior to testosterone initiation			
Stage I	3 (42.9%)	14 (58.3%)	14 (45.2%)
Stage II	4 (57.1%)	6 (25.0%)	12 (38.7%)
Stage III	0 (0%)	2 (8.3%)	2 (6.5%)
Unknown	0 (0%)	2 (8.3%)	3 (9.7%)
Testosterone indication			
Hypogonadism/low libido	6 (85.71)	20 (83.3%)	26 (83.9%)
Gender-affirmation	1 (14.3%)	2 (8.3%)	3 (9.7%)
Other	0 (0%)	2 (8.3%)	2 (6.5%)
Testosterone type			
Topical (gel, patch, or powder)	3 (42.9%)	15 (65.2%)	19 (61.3%)
Subcutaneous/implant	0 (0%)	0 (0%)	0 (0%)
Intramuscular	4 (57.1%)	9 (37.5%)	12 (38.7%)

ET, Exogenous testosterone; *HS*, hidradenitis suppurativa.

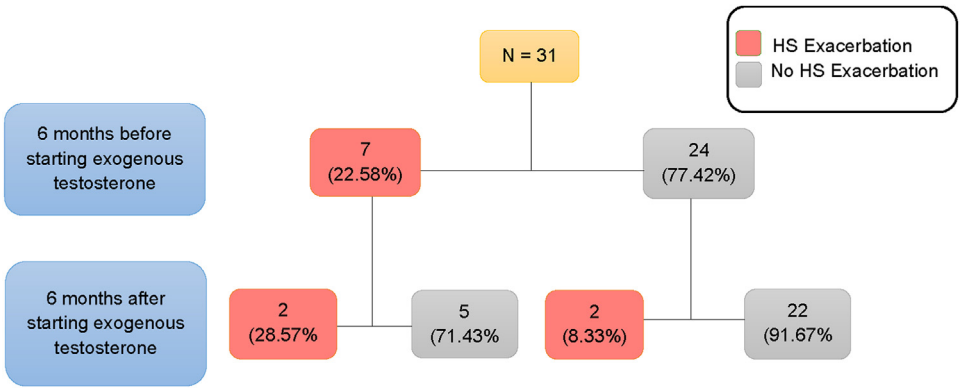

Fig 1. Number of patients with hidradenitis suppurativa disease exacerbation(s) before and after taking exogenous testosterone. The difference in the proportion of patients with hidradenitis suppurativa disease exacerbation (before vs after taking exogenous testosterone) was 9.7% (95% CI, −9.2% to 28.5%, $P = .51$). *HS*, Hidradenitis suppurativa.

IRB approval status: This study was approved by the Mass General Brigham IRB.

Data availability statement: Raw data were generated at Mass General Brigham (MGB). Derived data supporting the findings of this study are available from the corresponding author [AC] on request.

Key words: disease exacerbation; exogenous testosterone; gender affirming care; hidradenitis suppurativa; hypogonadism.

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Conflicts of interest

Dr Charrow serves on the Advisory Board for Novartis and has advised for Q32. Authors Kamal, Afzal, Ziad, and Santiago-Soltero have no conflicts of interest to declare.

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