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Long-Term Dermatological Considerations of the Vulva and Vagina in Transgender Women After Gender-Affirming Surgery

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Abstract

Emerging research has shed light on the long-term dermatological implications for transgender women following gender-affirming surgery, revealing an increased tendency towards conditions such as lichen sclerosus (LS), vulvar atrophy, and other cutaneous diseases affecting the vulva and vagina. Current literature emphasizes the need for comprehensive postoperative care and highlights the intricate relationship between hormonal changes, surgical interventions, and dermatological outcomes in transgender women. While existing studies offer valuable insights, gaps persist in our understanding of the precise mechanisms and risk factors associated with these postoperative dermatological conditions. Future research endeavors should focus on elucidating the pathways which influence the development of LS, vulvar atrophy, and related cutaneous diseases in transgender women, aiming to inform targeted preventive strategies and optimize the long-term health outcomes of this population. This review provides a foundation for advancing knowledge and underscores the importance of ongoing investigations into the dermatological well-being of transgender women following gender-affirming surgery.

Introduction

The dynamic field of transgender healthcare has had remarkable advancements, notably in the domain of gender-affirming surgeries for transgender women. Within this transformative landscape, emerging research illuminates a compelling narrative regarding the enduring dermatological implications subsequent to such surgical interventions. This comprehensive exploration reveals an increased vulnerability to dermatological conditions, specifically lichen sclerosus (LS), vulvar atrophy, and other cutaneous diseases affecting the vulva and vagina amongst transgender women. The intricate interplay between hormonal alterations, surgical interventions, and the ensuing dermatological outcomes underscores the imperative for a nuanced understanding to facilitate optimal postoperative care for this unique demographic. This review lays the foundation for an in-depth examination of the existing literature, accentuating discernible gaps in knowledge, and delineating the trajectory for future research endeavors.

The landscape of transgender healthcare is evolving with the increasing prevalence of gender-affirming surgeries, which are integral to aligning physical characteristics with gender identity [1, 2]. Within this transformative context, emerging research illuminates a previously overlooked aspect of comprehensive healthcare - the heightened susceptibility to dermatological conditions post-gender-affirming surgery in transgender women [3, 4]. Notably, recent studies have identified specific dermatological conditions, including LS, vulvar atrophy, and various cutaneous diseases affecting the vulva and vagina, which underscore the complexity of postoperative outcomes in this population [5, 6].

The interplay between hormonal changes, surgical interventions, and dermatological outcomes emerges as a significant focal point in understanding the comprehensive postoperative care needed for transgender women [7, 8]. Hormonal changes, particularly those associated with hormone replacement therapy (HRT), exert profound effects on the structure and function of the skin [9, 10]. Concurrently, surgical techniques such as vaginoplasty and vulvoplasty introduce anatomical alterations, potentially influencing the risk profile for dermatological conditions [3, 7]. These insights underscore the necessity of recognizing and comprehending the intricate connections between these variables for tailored and effective postoperative care.

While existing literature provides initial insights into the heightened vulnerability to dermatological conditions post-gender-affirming surgery, a more in-depth examination of the underlying mechanisms and risk factors is warranted [3, 4]. Gaps persist in our understanding, calling for rigorous exploration to inform evidence-based interventions. This scientific inquiry aligns with the imperative of further exploring the dermatological well-being of transgender women post-gender-affirming surgery [5, 10]. Through a more nuanced understanding of mechanisms and risk factors, we aim to contribute to the evolving body of knowledge and pave the way

for targeted preventive strategies, optimizing the long-term health outcomes of this demographic [2, 6].

Discussion

The extant literature underscores the pivotal role of postoperative care in mitigating dermatological challenges faced by transgender women, revealing a notable prevalence of lichen sclerosus (LS), vulvar atrophy, and related cutaneous diseases. A complex amalgamation of factors, ranging from hormonal shifts intrinsic to gender-affirming surgeries to the intricacies of surgical techniques employed, contributes to the heightened vulnerability observed in this population. While extant studies provide valuable insights into the prevalence of these conditions, a comprehensive understanding of the underlying mechanisms and modifiable risk factors remains elusive.

The unique dermatological challenges faced by transgender women following gender-affirming surgery necessitate a more granular examination of the interplay between hormonal shifts and surgical interventions. Recent studies highlight the multifaceted nature of hormonal changes, including the impact of HRT on the skin's structural and functional aspects. Additionally, surgical techniques, such as vaginoplasty and vulvoplasty, can introduce alterations to the genital anatomy, potentially influencing the risk profile for dermatological conditions. Despite these insights, gaps persist in discerning the precise mechanisms and delineating the specific contributions of hormonal versus surgical factors.

Dermatological Implications in Transgender Women

The study of dermatological conditions in transgender women, particularly following gender-affirming surgery or HRT, remains limited but has revealed significant health challenges, including LS and condyloma acuminata. LS is recognized as an autoimmune disorder characterized by chronic inflammation and thinning of the skin, with sex hormones and trauma also implicated as contributing factors [11]. This condition can lead to severe complications such as scarring, loss of standard vulvar architecture, tissue adhesion, sclerosis, tears, and subsequent loss of sexual function, alongside dysuria, constipation, itching, and soreness [12, 13]. McMurray et al. document a case of a transgender woman who developed anogenital LS eight years after gender-affirming surgery, presenting with several years of vulvar pruritus and burning pain [14]. Similarly, additional cases have reported the occurrence of LS in transgender women several years following gender-affirming surgery, suggesting surgical and hormonal interventions as significant contributors to the development of LS, highlighting the need to maintain continuity with patients who have undergone gender-affirming procedures due to the extended development of dermatologic conditions [15, 16, 17]. One noteworthy case revealed hair follicles present in an examined biopsy sample, indicating that the area affected by LS originated from scrotal skin, further illustrating the complexities of post-surgical dermatological outcomes [16]. These findings highlight the unique presentation of patients assigned male at birth in the context of hormone use, chronic irritation, trauma, and scarring [18, 19, 20, 21].

Condyloma acuminata is caused by the human papillomavirus (HPV) and emerges as another dermatologic challenge predominantly affecting non-keratinized epithelium [22]. The dynamic of HPV infection in transgender women is multifaceted, influenced by behavioral, biological, and healthcare-related factors. Numerous studies have documented neovaginal HPV, including high-risk strains, present within this population [23, 24, 25, 26]. Moreover, Singh et al. reveal that the prevalence of HPV from anal swabs was 88.6% among transgender women, substantially higher than the 70.9% prevalence among men who have sex with men (MSM) [27]. This risk is accentuated by the anatomical construction of the neovagina, often lined with scrotal or penile skin, predisposing these areas to HPV-related conditions [28]. The evidence of neovaginal HPV infection demands a multifaceted approach to healthcare for transgender women. This includes not only the enhancement of screening protocols but also the integration of comprehensive HPV vaccination programs tailored to address the specific needs and risks of the transgender population.

As previously mentioned, a complication arising from gender-affirming surgery includes hair growth development in the introitus as the tissue used, often from the scrotum, contains hair follicles. This can lead to pain, discharge, and serve as a nidus for infection. De Haseth et al., report a case series of five transgender women with symptomatic neovaginal candidiasis after penile inversion vaginoplasty; the environmental risk factors which are known to predispose individuals to the development of vaginal candidiasis such as diabetes mellitus, recent antibiotic use, and immunocompromisation are unknown risk factors for candida infection in neovaginas [29]. Another dermatological condition that can develop post-gender-affirming surgery includes the formation of scars [13]. Scars result after any cause of dermal injury and result in the proliferation of fibrous tissue. Keloid or hypertrophic scars can result and can be disfiguring to a transgender woman's ideal body image in addition to causing physical discomfort. These studies demonstrate the need for further, standardized reports on surgical techniques and outcomes if we are to be aware of the full gamut of dermatological conditions that may arise after gender-affirming surgery.

Estrogen HRT serves as a foundational element in the transition process for many transgender women, facilitating the development of female secondary sexual characteristics and aligning physical appearance with gender identity. The effects of estrogen HRT extend beyond feminization and can significantly impact the skin by enhancing thickness, hydration, and wound healing capabilities [30, 31]. However, post-surgical hormonal changes introduce complexities, including the pharmacological effects of exogenous hormones and alterations in the body's endogenous hormone production, particularly following interventions such as orchiectomy, which transgender women may pursue in the gender-affirming process [32].

Altogether, the dermatological conditions of the vestibule, such as LS and condyloma acuminata, in transgender women underscore the importance of long-term follow-up and dermatological screening for transgender women who have undergone gender-affirming surgery or who are receiving HRT. This need is further accentuated by the underreporting of incidence rates for such conditions, indicating a critical gap in dermatological surveillance within this population. Despite the valuable insights provided by the limited cases of LS, significant gaps remain in our understanding of the incidence, pathophysiology, and optimal management of LS and other dermatological conditions in transgender women post-gender-affirming interventions. Calls for larger, longitudinal studies are aimed at closing these knowledge gaps, developing targeted

prevention and treatment guidelines, and informing healthcare policy to better support the transgender community.

Mechanisms and Risk Factors of Dermatological Manifestations

While the concrete pathogenesis of vulvar LS remains under investigation, it appears to be largely dominated by immune and genetic targets [33]. The modifiable risk factors that influence vulvar atrophy and conditions such as LS are somewhat nebulous; the literature demonstrates associations between LS and the following factors: trauma, hormone levels, and certain medications [11]. Infections were previously believed to be a risk factor, but this has been disproved in more recent years. The most well-established factor contributing to LS presentation is the Koebner phenomenon, which is induced by chronic irritation and trauma [34]. Sources of friction, surgical intervention, and cuts or scrapes traumatizing the skin lead to the development of LS lesions along the sites of cutaneous interference. There have been some reports of LS in association with medications including carbamazepine, imatinib, pembrolizumab, nivolumab, and ipilimumab [11, 34]. Thus, as these therapies continue to multiply and their use becomes more widespread, they pose a risk for the development of cutaneous autoimmune diseases. There has been substantial discussion concerning Borrelia Burgdorferi, Hepatitis C, and HPV-16 as potential triggering infections for LS, however, these have all been investigated and disproved [11, 34]. The relationship between hormone levels and LS has not been proven in the literature, and there is insufficient evidence supporting the resolution of LS with testosterone, HRT, or contraceptive pills [34].

Histologic and Cellular Changes in LS

Histopathologic characterization of standard LS lesions features hyperkeratosis, epidermal atrophy, compact sclerosis (hyalinized and homogenized collagen) in the upper dermis with perivascular inflammatory and lymphocytic infiltrate in the dermis below [11, 33]. These are somewhat nonspecific findings and are shared with other cutaneous disorders, adding to the debate concerning the diagnostic features that compose LS. However, as the name sclerosus implies, the cellular-level changes seen in LS reveal a complex environment of genetic and immune phenomena regulating sclerotic tissue formation. Several autoimmune and genetic targets arise from the literature as areas for a prospective investigation into the molecular and histopathological insights into the cellular-level changes associated with LS and vulvar atrophy. A key, upstream genetic player of LS discussed in the literature is the increased expression of microRNA (miR)-155 in activated immune cells, which regulates sclerosis by increasing collagen synthesis and fibroblast proliferation [35]. Additionally, miR-155 is postulated to be responsible for activation of a Type 1 T helper (Th1)-mediated autoimmune response which inhibits regulatory T cell activity. This Th1 predominant response is supported by histologic evidence as T-cell infiltration of the dermis is a key feature of LS, involving primarily CD8+ and T-regulatory T cells, expressing the chemokine receptors CXCR3 and CCR5 [11]. Downstream activity of miR-155 includes downregulation of FOXO3 and CDKN1B, both of which promote fibroblast proliferation and increased collagen synthesis, and interleukin (IL)-10, an indicator of decreased T-regulatory cell function [35, 36]. Additional findings in patients with LS were a reduction in levels of anti-inflammatory IL-10, while pro-inflammatory cytokines such as tumor necrosis factor (TNF) and IL-6 levels were elevated when compared to healthy controls, demonstrating a propensity toward autoimmune dysregulation harming the body [33].

An additional piece of autoimmunity that has been demonstrated in the serum of individuals with LS are humoral antibodies toward the extracellular matrix protein (ECM)-1, which is key for structural integrity of the skin as it acts as an attachment point for various molecules within the dermal-epidermal junction [33, 37]. It is unclear whether ECM-1 dysfunction is a cause or effect of the disease process of LS, as it has also been demonstrated to have a vital role in genodermatosis, lipoid proteinosis, and does not favor the genital skin in patients affected by this condition [33, 38]. ECM-1 antibodies may play a role in the uptick of collagen synthesis seen in LS lesions, as these antibodies have been seen to activate metalloproteinase 9, a collagenase which acts to disrupt the basement membrane zone, activate transforming growth factor (TGF)-β, and increase collagen synthesis. Additionally, fibroblast activity and collagen synthesis may also be affected by the protein galectin-7 which has been shown in increased levels in LS, however its role is not clearly elucidated and requires further investigation [11, 33].

A final piece of the molecular framework described in the literature contributing to the histopathological changes observed in LS is the creation of reactive oxygen species (ROS). It is theorized that through the upregulation of pro-inflammatory cytokines there is increased release of ROS which fragment autoantigens, essentially creating new antigens for identification by humoral autoantibodies [33]. There is evidence indicating that oxidative stress may trigger p53, as it has been found to be overexpressed in the basal keratinocytes of LS [11, 33].

Psychosocial Impact of Dermatologic Conditions in Transgender Women

There is substantial literature demonstrating that vulvovaginal inflammatory dermatoses including LS, genital lichen planus, lichen simplex chronicus (LSC), and erosive vulvovaginal lichen planus, increase psychological distress and cause a reduction in the quality of life, inhibiting sexual functioning, and even cause pain during intercourse [11, 39, 40, 41, 42]. Unfortunately, due to the stigmatizing nature of discussing genital conditions, patients will often defer seeking treatment, and a late diagnosis of these conditions can produce greater frustration as high degrees of disease severity correlate with increased psychosexual burden, decreased quality of life, increased symptoms, and delayed treatment [42]. Women with vulvar LS have greater degrees of sexual dysfunction, are less sexually active, and can have persistent sexual dysfunction despite treatment [43]. Ranum et al. elucidate the fact that there are different aspects to assess when investigating LS and quality of life, such as physical symptoms, emotions related to genital disease such as shame and embarrassment, the impact of these cutaneous genital conditions on a patient's ability to perform activities of daily living, and overall impact on sexual function [44]. Further investigating how genital LS can impact these areas of life can assist clinicians in providing more patient-centered care as they treat individuals with LS. Many of the factors that contribute to reductions in quality of life could be improved upon with simple interventions, such as providing informational packets about their condition as well as continuity of care to allow patients to to feel supported in the management of their disease [45].

Strong evidence suggests a correlation between LS and mental health conditions such as depression, anxiety, and stress; one study found a prevalence of depression and comorbid vulvar inflammatory dermatoses ranging from 14 to 50% [40, 42]. A case-control study of 765 women with LS and 3060 age-matched controls from an NIH database demonstrated that women with LS are at statistically significant increased odds for having a diagnosis of comorbid depression (2.16-fold increase in odds) and anxiety (2.5-fold increase in odds) [39]. Prospective investigations of the psychosocial impact of LS on mental health and overall well-being would be beneficially informed by the limitations cited by these authors when constructing their studies, namely, the need to demonstrate the chronological nature between these associated diagnoses. Additionally, as pain during intercourse is a commonly described symptom that contributes to sexual dysfunction and reduced quality of life in patients living with LS, prospective studies should consider whether treatment of LS-associated pain will indirectly treat sexual dysfunction and improve quality of life. Prospective investigations into the psychosocial impact of vulvovaginal conditions such as LS need to include the evaluation of how these conditions affect transgender individuals, and racial and ethnic minority populations; little has been deduced specifically about their experiences and quality of life in comparison to non-minority populations living with LS [45].

Investigations should also be driven to evaluate dermatological conditions on mental health and well-being by specifically including a more discrete evaluation of the severity of disease and its correlation with mental health outcomes. Most prior literature investigating the impact of dermatological vulvovaginal conditions on mental health focused on assessing quality of life, depression, anxiety, and stress in individuals carrying the diagnosis, without accounting for disease severity [44]. Thus, to provide more effective, patient-centered care aimed to improve quality of life, it will be necessary to have interventions tailored to the specific needs of patients in relation to the severity of their needs at a certain disease stage.

Future Research Directions: Proactive Strategies and Longitudinal Studies

This review serves to enhance knowledge on the currently available research into dermatological conditions afflicting transgender women and known associated risk factors. However, future research initiatives should prioritize elucidating the intricate pathways connecting hormonal shifts, surgical interventions, and the elevated risk of dermatological conditions in transgender women. While current literature focuses on the conditions these women are faced with, a targeted exploration of the modifiable risk factors is imperative to develop proactive preventive strategies. Longitudinal studies are essential to discern the evolution of these conditions and to ascertain whether their prevalence changes with post-operative time. Moreover, rigorous investigations into the potential impact of adjunct therapies, such as postoperative topical interventions or adjustments to HRT regimens, could offer valuable insights into mitigating dermatological challenges.

In-depth molecular and histopathological investigations could shed light on the cellular-level changes associated with LS and vulvar atrophy in transgender women. These studies could delineate the specific mechanisms influenced by hormonal and surgical factors, providing a foundation for targeted interventions. Furthermore, prospective research should examine psychosocial aspects and explore the impact of these dermatological conditions on the mental health and overall well-being of transgender women post-surgery.

Future Considerations

Our comprehensive review delves into the vast and long-term dermatological effects of the vulva and vagina that are experienced by transgender women after gender-affirming surgery. While existing research offers some valuable insight into understanding the complex relationship between hormone changes, surgeries, and skin outcomes, there is still a need for a focused effort to fill knowledge gaps. Future studies should aim to prioritize uncovering the specific mechanisms behind these intricate variables, identifying factors that can be changed, and creating interventions to improve the long-term skin health of transgender women. This research aligns with the broader goal of ensuring that post-surgical care addresses the unique skin needs of this population in a thorough and personalized manner.

The development of ongoing studies is crucial to support the literature and leads to the development of universal guidelines and best practices in preventing the onset, diagnosing, treating, and preventing the recurrence of these dermatological concerns. This scientific inquiry is aligned with the broader objective of improving postoperative care for transgender women and addressing dermatological concerns related to the vulva and vagina. By investigating the dermatological implications of gender-affirming surgeries, this research aims to develop tailored interventions to enhance the long-term skin health of transgender women. This effort is crucial for establishing comprehensive and inclusive care protocols, ultimately improving health outcomes and quality of life for this population.

While such methods are not adequately documented in the medical literature, there is a steady increase in the literature addressing LGBTQ+ inequalities & inequities, particularly in the field of surgery in recent years, offering hope for more strides towards reducing disparities and promoting health equity among transgender patient populations [46]. To that end, this comprehensive review of the literature aims to inform tailored and effective interventions for the well-being of transgender individuals' post-gender-affirming surgery.

Conclusion

Our comprehensive review serves as a foundational exploration into the dermatological implications for transgender women post-gender-affirming surgery. While existing literature provides crucial insights, the complexity of the relationship between hormonal shifts, surgical interventions, and dermatological outcomes necessitates a concerted effort to bridge existing knowledge gaps. The trajectory of future research should focus on uncovering the precise mechanisms, discerning modifiable risk factors, and developing targeted interventions to optimize the long-term dermatological health of transgender women. This scientific inquiry aligns with the broader objective of ensuring that postoperative care is not only comprehensive but also tailored to the unique dermatological needs of this population.

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