

Vulvar Lichen Sclerosus: What's New?

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Vulvar lichen sclerosus (VLS) is an underserved area in medicine and dermatology. We discuss updates in VLS, which include the following: (1) development of core outcome domains to include in all future clinical trials, with current efforts focused on determining outcome measurements for each domain; (2) increased understanding of the impact VLS has on quality-of-life (QOL) outcomes; (3) expanded disease associations; (4) clinical and histologic variants, including vestibular sclerosis and nonsclerotic VLS; and (5) updates in management of VLS.

Core Outcomes Measures

The burden of VLS is challenging to quantify, with little agreement among experts.¹ Recently there has been a focus on developing scoring scales to measure disease progression and treatment response. Simpson et al² pioneered the development of a core outcome set to be included in all future clinical trials for genital lichen sclerosus (LS)—clinical (visible) signs, symptoms, and LS-specific QOL.

Although there is no standardized method for assessing disease severity, various scales have been proposed to measure clinical findings in VLS, such as the vulvar architecture severity scale³ as well as the clinical LS score,⁴ which is the only validated scale to incorporate the signs and architectural changes identified by a 2018 Delphi consensus group of the International Society for the Study of Vulvovaginal Disease.⁵ Work is ongoing to identify and evaluate outcome measurement instruments for each of the 3 core outcome domains.

Increased Understanding of QOL Impacts

Pain, pruritus, impairment of sexual function, genitourinary complications, architectural changes, and risk for squamous cell carcinoma (SCC) all have been well established as VLS sequelae.^{6,7} Recent studies have focused on

the QOL impact and associations with psychiatric comorbidities. A matched case-control study found that LS was significantly associated with depression and anxiety among US women ($P < .001$), and individuals with LS had a more than 2-fold increased odds of receiving a diagnosis of depression or anxiety.⁸

A review evaluating QOL outcomes in LS found that overall QOL was impaired. Female patients reported worse QOL in the work-school domain of the dermatology life quality index compared with male counterparts.⁹

Finally, a study exploring the experiences of patients living with VLS highlighted the secrecy and stigma of the condition,¹⁰ which serves as a call to action to improve the general population's knowledge about vulvar anatomy and create change in societal attitudes on vulvar conditions.

Although there are several instruments assessing vulvar-specific QOL, most are for patients with vulvar cancer and focus on sexual function. In 2020, Saunderson et al¹¹ published the 15-item vulvar quality of life index (VQLI), which has broad implications for measuring vulvar disease burden and is an important tool for standardizing vulvar disease measurements and outcomes for clinical research.¹² The VQLI, though not specific to VLS, consists of 4 domains to assess vulvar QOL including symptoms, anxiety, activities of daily living, and sexuality. Studies have evaluated this scoring system in patients with VLS, with 1 study finding that VQLI correlated with clinician-rated severity scores ($P = .01$) and overall patient itch/discomfort score ($P < .001$) in VLS.^{13,14}

Expanded Disease Associations

Lichen sclerosus has a well-known association with vulvar SCC and other autoimmune conditions, including thyroid disease and bullous pemphigoid.¹⁵⁻¹⁷ Recent studies also have revealed an association between LS and psoriasis.¹⁸ A case-control study from a single center found VLS was associated with elevated body mass index, statin usage,

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and cholecystectomy.¹⁹ Gynecologic pain syndromes, interstitial cystitis, urinary incontinence, and some gastrointestinal tract disorders including celiac disease also have been found to be increased in patients with VLS.²⁰ Finally, the incidence of cutaneous immune-related adverse events such as LS has increased as the use of immune checkpoint therapies as anticancer treatments has expanded.²¹ Clinicians should be aware of these potential disease associations when caring for patients with VLS.

The incidence of VLS is higher in lower estrogen states throughout the lifespan, and a recent case-control study evaluated the cutaneous hormonal and microbial landscapes in postmenopausal patients (6 patients with VLS; 12 controls).²² Levels of the following cutaneous hormones in the groin were found to be altered in patients with VLS compared with controls: estrone (lower; $P=.006$), progesterone (higher; $P<.0001$), and testosterone (lower; $P=.02$). The authors found that most hormone levels normalized following treatment with a topical steroid. Additionally, bacterial microbiome alterations were seen in patients with VLS compared with controls. Thus, cutaneous sex hormone and skin microbiome alterations may be associated with VLS.²²

Updates in Clinical and Histologic Variants

Less-recognized variants of VLS have been characterized in recent years. Vestibular sclerosis is a variant of VLS with unique clinical and histopathologic features; it is characterized by involvement localized to the anterior vestibule and either an absent or sparse lymphocytic infiltrate on histopathology.^{23,24} Nonsclerotic VLS is a variant with clinical features consistent with VLS that does not exhibit dermal sclerosis on histopathology. Thus, a diagnosis of nonsclerotic VLS requires clinicopathologic correlation. Four nonsclerotic histopathologic subtypes are proposed: lichenoid, hypertrophic lichenoid, dermal fibrosis without acanthosis, and dermal fibrosis with acanthosis.²⁵ Longitudinal studies that correlate duration, signs, and symptoms will be important to further understand these variants.

Management Updates

First-line treatment of VLS still consists of ultrapotent topical corticosteroids with chronic maintenance therapy (usually lifetime) to decrease the risk for SCC and architectural changes.²⁶ However, a survey across social media platforms found steroid phobia is common in patients with VLS ($N=865$), with approximately 40% of respondents endorsing waiting as long as they could before using topical corticosteroids and stopping as soon as possible.²⁷ Clinicians should be aware of possible patient perceptions in the use of chronic steroids when discussing this therapy.

Randomized controlled trials utilizing fractional CO₂ devices for VLS have been performed with conflicting results and no consensus regarding outcome measurement.^{28,29} Additionally, long-term disease outcomes following laser use have not been investigated. Although

there is evidence that both ablative and nonablative devices can improve symptoms and signs, there is no evidence that they offer a cure for a chronic inflammatory skin condition. Current evidence suggests that even for patients undergoing these procedures, maintenance therapy is still essential to prevent sequelae.³⁰ Future studies incorporating standardized outcome measures will be important for assessing the benefits of laser therapy in VLS. Finally, the reasons why topical corticosteroids may fail in an individual patient are multifaceted and should be explored thoroughly when considering laser therapy for VLS.

Studies evaluating the role of systemic therapies for refractory cases of VLS have expanded. A systematic review of systemic therapies for both genital and extragenital LS found oral corticosteroids and methotrexate were the most-reported systemic treatment regimens.³¹ Use of biologics in LS has been reported, with cases utilizing adalimumab for VLS and dupilumab for extragenital LS. Use of Janus kinase inhibitors including abrocitinib and baricitinib also has been reported for LS.³¹ A clinical trial to evaluate the safety and efficacy of topical ruxolitinib in VLS was recently completed (ClinicalTrials.gov identifier NCT05593445). Future research studies likely will focus on the safety and efficacy of targeted and steroid-sparing therapies for patients with VLS.

Final Thoughts

Vulvar lichen sclerosis increasingly is becoming recognized as a chronic genital skin condition that impacts QOL and health outcomes, with a need to develop more effective and safe evidence-based therapies. Recent literature has focused on the importance of developing and standardizing disease outcomes; identifying disease associations including the role of cutaneous hormones and microbiome alterations; characterizing histologic and clinical variants; and staying up-to-date on management, including the need for understanding patient perceptions of chronic topical steroid therapy. Each of these are important updates for clinicians to consider when caring for patients with VLS. Future studies likely will focus on elucidating disease etiology and mechanisms to gain a better understanding of VLS pathogenesis and potential targets for therapies as well as implementation of clinical trials that incorporate standardized outcome domains to test efficacy and safety of additional therapies.

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