Incidence of Vulval squamous cell carcinoma in women with vulval lichen sclerosus in an Australian tertiary referral centre

Authors: Meani R¹, Howard A¹, Veysey E¹

¹Department of Dermatology Royal Women's Hospital Melbourne, Victoria, Australia.

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Correspondence:

Dr Rowena Meani

Skin and Cancer Foundation Inc.

Level 1, 80 Drummond Street, Carlton, Victoria, Australia, 3053

Phone: (03) 9623 9464 Fax (03) 9623 9444

Email: meani.rowena@gmail.com

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Vulval lichen sclerosus (VLS) is associated with two significant complications: development of genital squamous cell carcinoma (SCC) and scarring with loss of vulval architecture and normal function.³ Reported SCC rates range from 1-6%.^{1,3,4,5}

Current treatment guidelines recommend the use of super-potent topical corticosteroid once or twice daily for 4 weeks then alternate days for 4 weeks then twice weekly for 4 weeks before review.⁶ There is little evidence or consensus on best practice for maintenance therapy.^{6,7} A recent study demonstrated significantly reduced SCC incidence in patients compliant with at least 3 times per week topical corticosteroid application regardless of symptoms (0%) compared to partially compliant patients (4.7%).⁷

Treatment guidelines for women with VLS attending the tertiary referral vulval clinic at our hospital, recommend standard initiation therapy with a super-potent topical corticosteroid for achieving disease control⁶ then maintenance therapy using the minimum topical corticosteroid required to remain symptom free and have no evidence of active disease (purpura, hyperkeratosis, fissures) at 4-12 monthly follow-up. We conducted a retrospective single-centre review of all patients seen with VLS 10th July 2012 through 5th April 2016 to determine the incidence of vulval intraepithelial neoplasia (VIN) or SCC.

504 patients with clinically or histologically confirmed diagnosis of VLS were seen during the study period. Patients with VIN or SCC at presentation were excluded (38). The mean age of VIN/SCC diagnosis was 65 years (56-77). A total of five women developed VIN/SCC, of which two developed differentiated VIN, two usual-type VIN and one SCC developing from usual-type VIN (Table 1). The incidence of VLS associated VIN was 2/466 (0.4%) and none developed VLS associated SCC. The mean time to development of VIN/SCC during routine follow up was 4.5 years (0.5-8 years). The patient who developed SCC was treated for VLS two and eight years prior to developing usual-type VIN and SCC respectively. All five patients were being followed up six monthly and used topical corticosteroid at least twice weekly (Table 1).

The incidence of VLS associated VIN/SCC in our cohort was 0.4%, which is considerably lower than previously reported (1-6%).^{1,3,4,5} Carlson and colleagues reported a pooled incidence of 4.5% (140/3093) from 22 studies.⁸ More recent studies report much lower SCC incidence rates from 1.4% to 2.7%.^{9,10} Lee et al. reported an incidence of 0% during long term follow up of 357 women who were compliant with long-term maintenance topical corticosteroid treatment over 4.7 years.⁷

The etiology of vulval SCC is not fully understood; known risk factors include VLS, human papilloma virus (HPV) infection, history of VIN and smoking.^{8,9,10} Other possible risk factors include disease severity, response to treatment, genetic predisposition and immune status.¹⁰ SCC in the setting of VLS is associated with differentiated VIN and considered unrelated to HPV.⁹ Women with VLS and differentiated VIN carry a greater risk of developing SCC.⁹ In our study only two developed VLS associated differentiated VIN and three HPV associated usual-type VIN, one of which went on to develop SCC.

This study has several limitations that may have resulted in an underestimate of VIN/SCC incidence. Firstly, including patients with a clinical rather than pathologically confirmed diagnosis of VLS. This may have lead to the inclusion of patients with vulval conditions that carry less carcinogenic risk. Biopsies were performed in the setting of diagnostic uncertainty and the risk of misclassification is unlikely to have influenced the results significantly. Secondly, loss to follow up; hospital records were searched to identify those presenting to other departments within the hospital in order to maximize capture of SCC cases regardless of failure to attend at the vulval disorders clinic. Finally, inadequate length of study period (3.8 years) to capture SCC development, however this is comparable with follow-up periods in previous studies ranging from 4.7 to 6.2.^{1,3,5,7} Further limitations include its retrospective design and lack of individual patient data. Consequently it is not possible to make inferences on causality or independent risk or protective factors for the development of SCC, which would require a prospective observational study design. In addition, the data reflects a tertiary referral centre population, thus including women with more severe disease. This is more likely to result in an increased incidence of SCC, which was not detected.

In conclusion, management of VLS within our hospital vulval disorders clinic with intensive initiation therapy and the minimum topical steroid required for maintenance, is associated with a low to negligible incidence of VIN (0.4%) and SCC (0%). However, no conclusions can be drawn on which elements of care or patient related factors might be responsible for this finding.⁷

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Table 1. Clinical characteristics of the five cases who developed VIN/SCC during follow up

Age at diagnosis	Diagnosis	Follow-up duration prior to diagnosis SCC/VIN (years)	Biopsy proven LS	HPV status	Duration of symptoms prior to presentation at RWH (years)	TCS regimen	TCS used
77	SCC moderately differentiated	8	Yes	Positive	30	daily	Clobetasol propionate 0.05%
56	VIN differentiated	6	Yes	Unk	Unk	2x week	Betamethasone dipropionate OV 0.05%
62	VIN differentiated	3	Yes	Unk	1	daily	Clobetasol propionate 0.05%
50	VIN usual type	0.5	Clinical diagnosis LS	Positive	2	2 nd daily	Methylprednisolone aceponate 0.1%
65	VIN usual type	5	Yes	Positive	Unk	2 nd daily	Methylprednisolone aceponate 0.1%

VIN, Vulval intraepithelial neoplasia; SCC, squamous cell carcinoma; OV, optimised vehicle;

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Author/s:

Meani, R;Howard, A;Veysey, E

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