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ORIGINAL ARTICLE

Vulvar lichen sclerosus in women is associated with lower urinary tract symptoms

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Abstract
Introduction and hypothesis Lichen sclerosus (LS) is thought to be primarily a disease of postmenopausal women. Little is reported about lower urinary tract symptoms (LUTS) in association with LS. The aims of this study were to evaluate the odds of having LS-associated LUTS and to identify the predominant type of LS-associated bladder dysfunction.
Methods This was a cross-sectional study with two cohorts investigating the association between LS and LUTS and the predominant type of LS-associated bladder dysfunction.
Results The odds of LUTS in women with LS were more than four times higher than in women without LS (OR 4.5, 95% CI 2.6–8.0; $p < 0.0001$). There was no significant difference in the occurrence of LUTS between women who experienced the first LS symptoms before and after the age of 50 years (36% and 53%, respectively, $p = 0.14$), or in the occurrence of the different types of LUTS between women with and without LS ($p = 0.3$). The most common type of LUTS was overactive bladder (OAB) in both women with LS (67.3%) and without LS (60%). The most prevalent type of LS-associated LUTS was OAB.
Conclusions The odds of developing LUTS (self-reported) are four times higher in women with LS than in those without. The predominant type of LUTS in women with and without LS is OAB.

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Introduction

Lichen sclerosus (LS) predominantly affects the anogenital area in women. The etiology is unknown. Histologically, an inflammatory infiltrate composed mainly of T lymphocytes and hyalinization of the upper dermis are found beneath the epidermis [1–4]. At the time of diagnosis most women are postmenopausal and already have advanced disease. It is therefore assumed that the onset of the disease is much earlier (5 to 15 years earlier is suspected) [5–7]. Some data suggest that LS is strongly associated with numerous bladder, bowel and pain comorbidities [8]. However, the association between LS and lower urinary tract symptoms (LUTS) and the characteristics of potential LS-associated LUTS have not yet been established [6, 8, 9].

The aims of this study were to evaluate the odds of having LS-associated LUTS and to identify the predominant type of LS-associated bladder dysfunction. The hypothesis tested was that the odds of LUTS are significantly higher in women with LS. The association between LS and LUTS was also evaluated.

Materials and methods

Study design

We performed a two-population cross-sectional study in cooperation with the "Verein Lichen sclerosus" (VLS; the German-speaking patient association for LS). Women were recruited from the VLS, and from the Unit for

Urogynecology and the Vulva Clinic of our tertiary referral hospital, the Cantonal Hospital of Lucerne, Switzerland. Between January 2013 and January 2015, data from all consecutive women attending the above clinics were included in the following four cohorts:

Cohort A consisted of women from the VLS who were diagnosed with LS either by biopsy or clinically by a private gynecologist or dermatologist. The VLS members were asked to complete a self-administered questionnaire. The following data were collected: current age, age at the time of first symptoms, age at diagnosis and the presence of LUTS (yes/no). No further details of their medical records were obtained. Male patients, children, and women younger than 18 years were excluded from the study.

Cohort B consisted of women without LS who were included to evaluate the occurrence of bladder dysfunction in women without vulvar disease. Women attending our general gynecological outpatient clinic for any reason other than vulvar disease were interviewed concerning ongoing bladder dysfunction (LUTS) including the question: "Do you have any symptoms of bladder dysfunction?" (yes/no).

Cohort C consisted of women from our specialized vulva clinic with confirmed LS (LS score ≥4 and/or confirmed by biopsy) [10] who reported the presence of LUTS. All women underwent a urogynecological examination in our urogynecology unit according to a defined protocol to determine the type of LUTS.

Cohort D consisted of all women with LUTS but without LS or any other vulvar disease recruited from our urogynecology unit. Women in cohort D underwent the identical exmamination to that performed in women of cohort C.

Cohorts C and D underwent a standardized urogynecological assessment. To obtain subjective data on LUTS all women in cohorts C and D completed the validated German Female Pelvic Floor Questionnaire (GFPFQ), which includes bladder, bowel, prolapse and sexual function domains [11]. Subjective symptoms were recorded including stress urinary incontinence (SUI), overactive bladder (OAB) with or without urinary incontinence, voiding dysfunction, recurrent urinary tract infections (UTI) or painful bladder syndrome (PBS; a multiple diagnosis was possible).

In women with LUTS and LS (cohort C) and women of cohort D comprehensive multichannel urodynamic studies were performed to provide an objective evaluation of the symptoms. The urodynamic studies included conventional filling cystometry (with maximal bladder filling to 500 ml), and a pressure flow study according to the recommendations of the International Continence Society (ICS) [12]. Residual urine was measured, and the clinical cough stress test and/or a pad weight test were performed to assess SUI with and without prolapse reduction. The examinations were followed by cystoscopy. Pathological findings including bladder calculi, signs of interstitial cystitis such as Hunner's ulcers or petechial bleeding were noted. The Pelvic Organ Prolapse Quantification (POP-Q) system was used in accordance with the recommendations of the ICS to assess the degree of pelvic organ prolapse (POP) [13]. The objective results were recorded as SUI, OAB with or without urinary incontinence, voiding dysfunction, current UTI and PBS (a multiple diagnosis was possible). OAB with or without urinary incontinence and voiding dysfunction was defined according to the standardized terminology of the International Urogynecological Association and the ICS. A postresidual volume of >100 cm^3 was regarded as elevated [14].

The study was approved by the Ethics Committee of Northwestern and Central Switzerland (EKNZ 2015–145) and written consent was obtained from each patient.

Statistical analysis

In cohort C, the occurrence rates of objective and subjective symptoms were combined to provide a total occurrence rate. The results are summarized as counts and percentages or medians and 95% confidence intervals (CI) as applicable. The 95% CI of the occurrence rates were calculated using the Clopper–Pearson exact binomial method. Fisher's exact test was used to test the differences in the observed frequency distributions among the cohorts and to calculate the odds ratios (OR) and their 95% CI. A p value <0.05 was considered statistically significant. Data were analyzed using the statistical software SPSS, version 22 (IBM Corp., Armonk, NY).

Results

Of 138 members of the VLS contacted, 113 responded. The data from 16 respondents (two men, four children and ten women with no LUTS data) were excluded from the analysis. Thus, the data from 97 women (cohort A) were evaluated. Six women did not remember the time of the first occurrence of LS symptoms. The majority of women (49/91, 54%) had their first symptoms of LS before the age of 50 years. The probability of the LS diagnosis before the age of 50 years was 61% (59/97, 95% CI 50–71%), significantly ($p = 0.04$) greater than 50%, as shown in Fig. 1 and 2.

A total of 44% of women (43/97) with LS reported LUTS (cohort A). There was no significant difference in the occurrence of LUTS between women who experienced the first LS symptoms before and after the age of 50 years (15/42, 36%, and 26/49, 53%, respectively; $p = 0.14$), or between women who were diagnosed with LS before and after the age of 50 years (22/54, 41%, and 16/43, 37%, respectively; $p = 0.7$).

The age-matched control group comprised 267 women with LUTS but without LS (cohort B). The data from 12 women (11 younger than 20 years and one with no data regarding LUTS) were excluded from the analysis. A total of

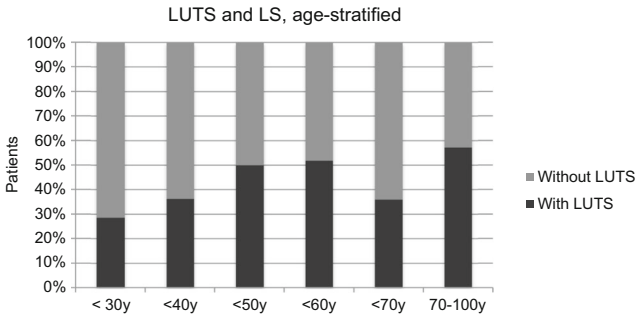

Fig. 1 LUTS in patients with assumed LS (from the VLS, cohort A; n = 97) stratified according to age

15% of women (38/255) without LS reported LUTS (Fig. 1 and 2). The odds of LUTS in women with LS (cohort A) were more than four times higher than in women without LS (cohort B; OR 4.5, 95% CI 2.6–8.0).

Cohort C comprised 113 women with LUTS and confirmed LS. Cohort D comprised 260 women with LUTS but wihtout LS. The results of the GFPFQ showed more severe bladder symptoms for the bladder domain in cohort D (score 123) than in cohort C (score 83) and for the bowel domain (score 56 and 208, respectively). Women in cohort C were not aware of any prolapse symptoms, in contrast to women in cohort D (score 257). The types of LUTS in the women investigated are shown in Table 1. The most common type of LUTS was OAB that was seen in both women with LS (76/113, 67.3%) and women without LS (156/260, 60%). In the urodynamic analysis, detrusor overactivity was seen in 17 patients in cohort C and in 13 patients in cohort D. Bladder hypersensitivity was seen in 51 patients in cohort C and in 22 patients in cohort D.

There were no significant differences in the occurrence of SUI, OAB, voiding dysfunction, UTI and PBS between women with and without LS (cohorts C and D; $p = 0.3$). Women with subjective and those with objective PBS showed severe petechial bleeding on cystoscopy that was confirmed by pathological analysis as increased numbers of mast cells in the urothelium. However, POP was present more frequently in women without LS (157/260, 60.4%) than in those with LS (4/113, 3.5%; $p < 0.0001$). Figures 3 and 4 show the numbers

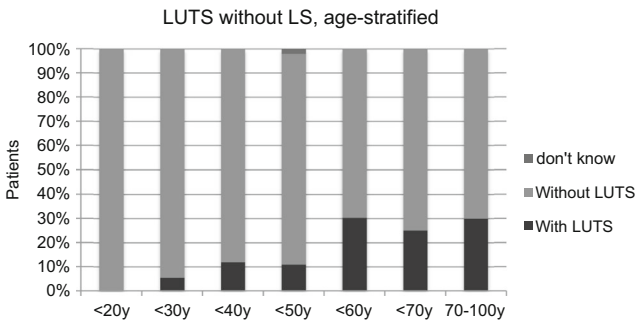

Fig. 2 LUTS in patients without LS (cohort B, n = 267) stratified according to age

Table 1 Types of LUTS in women with LS (cohort C) and without LS (cohort D). A multiple diagnosis was possible

	Cohort C (n = 113)	Cohort D (n = 260)
Stress urinary incontinence	26 (23.0%)	86 (33.1%)
Overactive bladder/detrusor overactivity	76 (67.3%)	156 (60.0%)
Voiding dysfunction	7 (6.1%)	13 (5.05)
Pelvic organ prolapse	4 (3.5%)	157 (60.4%)
Urinary tract infection	21 (18.6%)	40 (15.4%)
Painful bladder syndrome	0	2 (0.8%)

of women with each type of LUTS in cohort C (with LS) and cohort D (without LS) stratified according to age.

Discussion

This study suggests that the odds of LUTS are significantly higher in women with LS. However, there was no significant difference in the characteristics of the LUTS between women with and without LS, although it tended to have peak onset in women after the age of 50 years. The predominant type of LUTS in women with and without LS was OAB. The majority of women (61%) were diagnosed with LS before the age of 50 years.

One major weakness of this study was that not all patients in cohort A had proven LS, and it is possible that some had another vulvar disease such as lichen planus or lichen simplex chronicus [15, 16], and there may have been selection bias. Furthermore some demographic data including demographic parameters and data on previous pelvic floor surgery, which could have been highly relevant, were lacking due to the diversity of the cohorts. These parameters will be included in a follow-up study

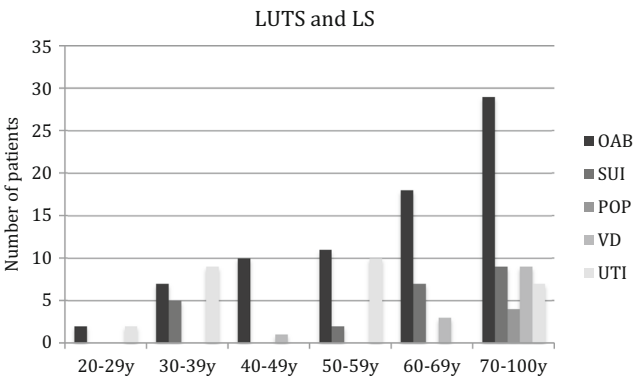

Fig. 3 Numbers of patients with each type of LUTS in cohort C (with LS; n = 113) stratified according to age. More than one type of LUTS in the same patient is possible (*OAB* overactive bladder ,*SUI* stress urinary incontinence, *POP* pelvic organ prolapse, *VD* voiding dysfunction, *UTI* urinary tract infection)

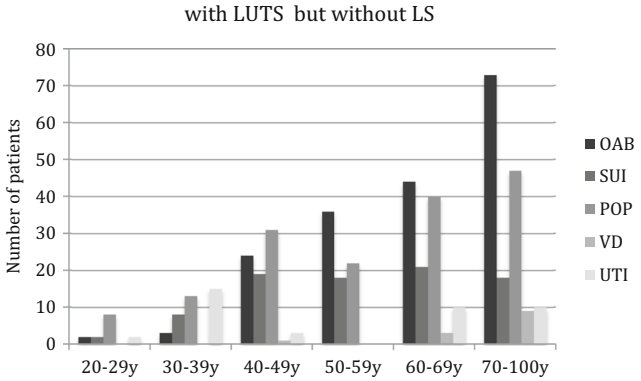

Fig. 4 Numbers of patients with each type of LUTS in cohort D (without LS; $n = 260$) stratified according to age. More than one type of LUTS in the same patient is possible (*OAB* overactive bladder ,*SUI* stress urinary incontinence, *POP* pelvic organ prolapse, *VD* voiding dysfunction, *UTI* urinary tract infection)

comparing cohort C and cohort D. For cohorts A and B questions on vaginal or bladder pain and symptoms of prolapse should have been more precise.

Our findings do not match those of Berger et al. who found that the prevalence of self-reported OAB (15%) in women with vulvar LS is less than in the general population in which the prevalence is approximately one third [8, 17, 18]. We found no significant difference in the prevalence of OAB between women with and without LS (cohorts C and D). However, the prevalence of concomitant OAB in women with LS was twice that in the general population. Furthermore, Kennedy et al. found that the prevalence of urinary incontinence in women with LS was lower than in controls [8, 9, 17, 18]. The risk of developing SUI seems to be no different in patients with LS compared to patients with no vulvar disease [9], in accordance with the results of our study. |However, some data suggest that women with LS are at relevant risk of PBS or irritable bowel syndrome. We were not able to confirm that PBS is commonly associated with LS [9]. However, some women with LS and LUTS reported symptoms of recurrent UTI which could not be objectively confirmed by urine analysis. It is possible that women with early stage LS and/or confirmed LS suffer from symptomatic non-bacterial bladder infection which might be one of the early symptoms of active LS, and this requires further evaluation. To date there is no evidence in the literature.

The prevalence of POP was higher in cohort D than in cohort C. From observation, women with LS seem to have firmer pelvic floor muscle than women without LS, but this observation is not evidence-based. Furthermore, we would expect a large number of women with POP in a urogynecology clinic so that selection bias would be present if these women were included in a comparative trial. This observation needs evaluation.

With the knowledge that there is an association between LUTS and LS, further prospective evaluation of the treatment of women with vulvar LS regarding symptomatic LUTS is warranted. Adequate treatment options for patients with LS and concomitant LUTS especially OAB need to be evaluated. In particular, it is not clear if adequate topical treatment of vulvar LS has an impact on LS-associated LUTS including OAB.

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Compliance with ethical standards

Conflicts of interest None.

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