Lichen Sclerosus and Urethral Stricture Disease – Identifying Risk Factors for Lichen Sclerosus Associated Urethral Stricture Disease - A Prospective Single Center Study

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ABSTRACT

Introduction and Objectives. Lichen sclerosus is a chronic inflammatory condition that usually affects the genital and anal areas. It causes irritation, skin changes, itching, and pain, often the foreskin gets tighter and more difficult to retract, leading to painful erections and bleeding during intercourse. The etiology is still unknown, is not caused by an infection, and cannot be passed to a sexual partner.

Materials and Methods. During the period January 1st, 2016 – to January 1st, 2017 we selected 137 patients with the diagnosis of urethral stricture disease and were candidates for urethroplasty. Patients were followed rigorously for 2 years after the surgery with uroflowmetry, measurement of post-void residual urine volume, IPSS, and IPSS QoL. For stricture recurrence confirmation the patients underwent retrograde urethrography. Other data used were weight, height, body mass index and established etiology of the urethral stricture, and age of patients at enrolment.

Results. Only 18 patients had definitive criteria for clinical diagnosis of LS, and out of these, 17 were circumcised. The relationship between BMI and LS was not statistically sustainable in our study results. Studies suggest that the lichen sclerosus has a more severe evolution in older patients, and we managed to demonstrate a statistically significant relationship between the age of the patient and the LS.

Conclusions. The treatment of urethral strictures in patients with confirmed lichen sclerosus is two-stage buccal mucosa graft urethroplasty. Urethral stricture disease in combination with LS appears to be a much more common and challenging disease and requires particular care.

Key-words: lichen sclerosus, urethral stricture, body mass index, urethroplasty

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INTRODUCTION AND OBJECTIVES

Lichen sclerosus (LS) is a chronic inflammatory and scarring disease of the skin of unknown etiology. The most common site of involvement is the ano-genital region. Male patients often present with white penile lesions or plaques, pruritis, painful erections and voiding, and bleeding or ulceration with intercourse. In severe cases, the foreskin thickens and can become phimotic, with development of urethral strictures. In women, the most common anogenital symptoms include pain, vulvar pruritis, dysuria, and dyspareunia[1].

LS is a chronically relapsing disease with a potential for atrophy, destructive scarring, functional impairment, and malignant evolution. Therefore, early diagnosis, prompt treatment, and long-term follow-up of affected patients are mandatory. Spontaneous remissions are rare[2].

LS can not be cured, but can be controlled by adequate treatment. With early treatment, long-term sequelae such as destruction of anatomic structures and progression to squamous cell carcinoma (SCC) may be prevented. For the affected patients it is essential that dermatologists, gynecologists, urologists, histopathologists, surgeons, general practitioners, and pediatricians, respectively, have a solid knowledge of the disease and will not hesitate to cooperate if required. Since LS begins with uncharacteristic symptoms, a meticulous clinical examination, raising the clinical suspicion and, if necessary, a histopathologic confirmation is required[3].

Although histologic descriptions and clinical diagnoses of LS date back to the mid-20th century, the pathophysiological mechanism remains largely elusive. Laboratory studies in the last decade have focused on finding molecular targets for treatment of LS[4].

There are several cited risk factors for lichen sclerosus in the current literature. The most common of them all is the lack of circumcision in male patients[5]. Injury to genital skin can increase the risk of LS as can friction, genital piercings for jewelry, and surgery[6].

An investigation into LS and medical comorbidities demonstrated an association between LS and higher mean body mass index (BMI) (31.0 vs 28.1, p = 0.001), diabetes mellitus (odds ratio [OR] = 2.04, p = 0.03), and a weaker association with coronary artery disease (OR = 1.88, p = 0.05)[7]. This finding is corroborated by additional studies, which have demonstrated an association between LS and BMI, diabetes mellitus, tobacco usage, hyperlipidemia, and hypertension.

We as urologist, are interested in identifying and managing lichen sclerosus since in locally advanced cases, on important complication of LS are urethral strictures. These are a bothersome and often hard to treat pathology.

The aim of this study is to identify patients with lichen sclerosus in a population of patients that are diagnosed with urethral strictures and require surgical intervention. We will also attempt to identify risk factor in patients that have LS and urethral strictures like BMI and

MATERIALS AND METHODS

We enrolled 137 patients from January 1st, 2016 – to January 1st, 2017, that were diagnosed with urethral stricture disease and were candidates for urethroplasty. Inclusion criteria were the diagnosis of urethral stricture and at least one prior endoscopic management of the urethral stricture. Patients were prospectively enrolled and followed up for 2 years after the surgery with uroflowmetry, measurement of post void residual urine volume, IPSS and IPSS QoL, and if any suspicion of failure was identified (Qmax < 15 ml/s, PVR > 100 ml, or increase in IPSS scores) then retrograde urethrography was performed to confirm stricture recurrence.

For this paper we will use clinical examination data obtained at enrollment, weight, height, body mass index and established etiology of the urethral stricture, and age of patients at enrolment.

The objective is to identify the number of patients that had lichen sclerosus induced urethral strictures and to identify if there is a statistically significant correlation between lichen sclerosus and body mass index or with age.

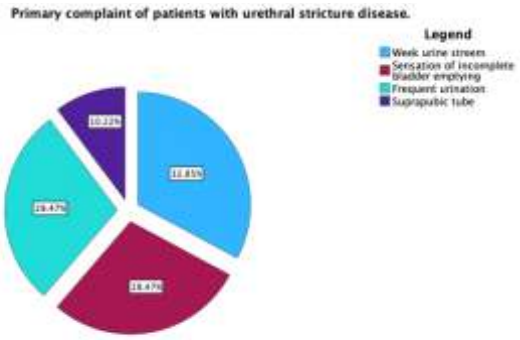
RESULTS

In our study population of 137 patients, mean age of patients was 48.62 years with a minimum of 18 years and a maximum of 79 years. Mean weight of patients was 91.8 kg, with a minimum of 58 kg and a maximum of 134 kg. Mean height was 1.77 m and mean calculated body mass index was 29.25 kg/m^2.

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Weight	137	58.00	134.00	91.81	18.74
Height	137	1.62	1.90	1.77	.06
BMI	137	17.44	42.59	29.25	5.94
Age	137	18.00	79.00	48.62	15.31
Valid N (listwise)	137				

Upon enrollment patients were asked what was the most bothersome symptom they had in regard to the urethral stricture disease.



Patients' response was recorded and represented in the above pie chart, that shows that most patients reported week urine stream as the main bothersome symptom they had, with a percentage of 32.85%. Other reported bothersome symptoms can be observed in the above pie chart and include sensation of incomplete bladder emptying and the presence of a suprapubic tube.

On clinical examination of the external genial area, in which we examined the patient's penis, prepuce, scrotum and perineum, we found that 18 patients (13.1%) had a highly suggestive exterior aspect for lichen sclerosus, and 7 (5.1%) patients had a scarred penis due to prior penile surgery.

Clinical Examination of Penis	N	%
Normal penis	112	81.7%
Lichen sclerosus	18	13.1%
Scarred penis	7	5.1%
Clinical Examination of the Pr	**N**	**%**
Present	107	78.1%
Absent - Circumcision	26	19.0%
Dehiscent - hipospadias	4	2.9%
Clinical Examination of the Sc	**N**	**%**
Normal	127	92.7%
Scarred	6	4.4%
Clinical Examination of the Pe	**N**	**%**
Normal	128	93.4%
Scarred - posttraumatic	4	2.9%
Scarred - previous urethroplasty	5	3.6%

The rest of the clinical examination of the external genial area can be observed in the above table, and we consider this information to be highly valuable because it weighs in on the clinical decision process, regarding the surgical procedure that is going to be used to reconstruct the stenosed urethra.

After identifying the number of patients with lichen sclerosus from our study population we would like to test the hypothesis that lichen sclerosus has more aggressive evolution with age and body mass index, as evidence suggest[8].

	Clinical Examination Prepuce			Total
	Present	Absent - circumcision	Dehiscent - hipospadias	
Normal	98	0	0	98
Lichen Sclerosus	1	17	0	18
Scared Penis	0	3	4	7

In Tabel 3, we see a crosstabulation representation of the clinical examination of the penis and prepuce, and we that 17 out of the 18 identified lichen sclerosus cases are circumcised. This probably to the widespread notion that circumcision is somehow curative of lichen sclerosus. There is no such evidence to support this claim, however there is evidence that circumcision is protective of developing lichen sclerosus, but the two scenarios are not the same thing[5,6].

Performing a Spearmans correlation on the above date, we obtained a value of 0.77 and a $p<0.01$ that was to be expected and only goes to prove that most circumcision in lichen sclerosus patients were done with therapeutic intent, either for phimosis or to treat lichen sclerosus.

Testing to see if we can identify age or body mass index as risk factors for severe lichen sclerosus, we performed statistical independent t test for age and BMI and clinical examination result of the penis.

	Clinical Examination Penis	N	Mean	Standard Deviation
Age	Lichen Sclerosus	18	55.88	9.22
	Normal Penis	98	48.13	15.47

Tabel 4 shows mean age of patients with lichen sclerosus and of those with normal looking penis on clinical examination. Those with lichen sclerosus have and higher mean age of 55.8 years.

		Levene's test		t-test						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
A	Equality of variance assumed	7.10	0.009	2.05	114	0.042	7.75	3.77	0.28	15.23
	Equality of variance not assumed			2.89	37.39	0.006	7.75	2.67	2.33	13.17

Result of Levene's test for equality of variances is $F=7.1$, $p < 0.009$. This means that the variances of the two groups are not assumed, and that all the criteria for performing an independent t test have been respected. Thus $t(37.39) = 2.89$, $p < 0.006$ with a 95% CI [2.33 – 13.17]. This result should be interpreted as highly statistically significant, and that prove there is a direct correlation between age and a more aggressive form of lichen sclerosus, that lead to severe urethral stricture involvement.

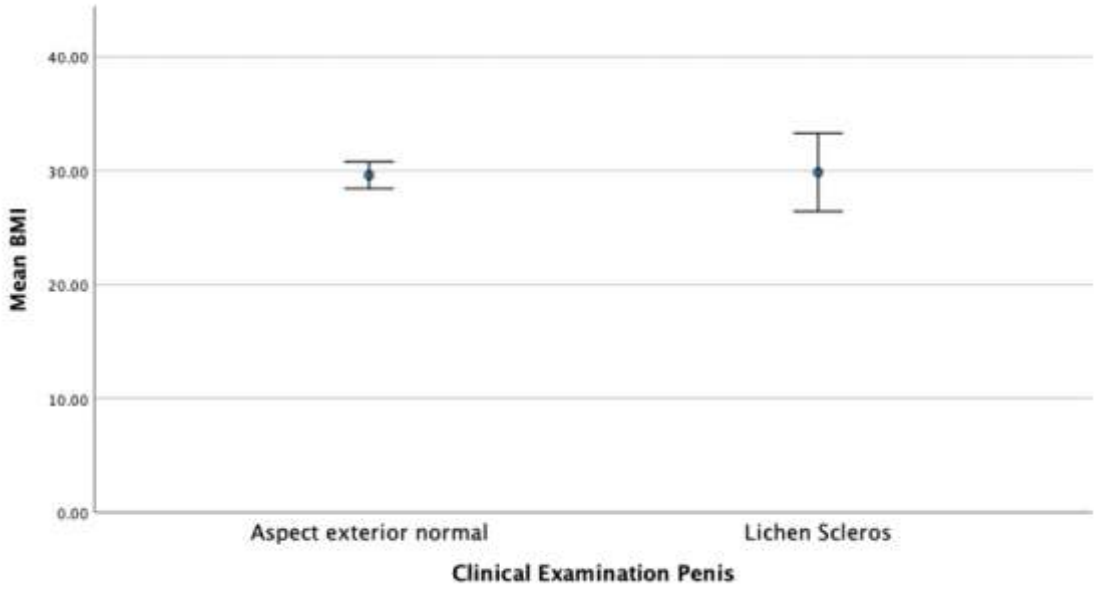
The other hypothesis is that between lichen sclerosus and increased body mass index are more frequently associated and will induce a more severe outcome. Testing in a similar manner, the relationship between the clinical examination result of the penis and body mass index by applying an independent t test, we observe that the mean BMI values of the two groups are similar, as seen in Table 6.

	Clinical Examination Penis	N	Mean	Standard Deviation
BMI	Lichen Sclerosus	18	29.86	6.87
	Normal Penis	98	29.60	5.85

As we execute the independent t test, Levene's test must be performed to know how to interpret the results and if we assume, or not, equality of variances.

		Levene's test for equality of variances		t test					
		F	P Value	t	df	P Value	Mean Difference	Mean Std. Error	95% CI
BMI	Equal variance assumed	0.28	0.594	0.16	114	0.869	0.25	1.54	-2.80 3.31
	Equal Variance not assumed			0.14	21.76	0.884	0.25	1.72	-3.32 3.83

Levene's test has a value of F = 0.28, p = 0.594 and this means that the variances are similar, and we must interpret the results of the independent t test with the assumption of equal variances. Thus t (114) = 0.16, p = 0.869, meaning that in our study group, there is no statistically provable relationship between BMI and lichen sclerosus.



Visual analysis of the relation between clinical examination result and BMI, is seen in the above graph, and is clear that the differences are not important. This was done to make sure that independent t test results were accurate.

DISCUSSIONS

Lichen sclerosus is an inflammatory dermatosis that has a chronic evolution, insidious onset, and without a known cure, or effective way to treat it. Urethral stricture disease is a complex urological disease that in association with lichen sclerosus can complicate treatment decisions, limit technical choices, and have a less favourable outcome on urethroplasty results[9].

The diagnosis of urethral stricture in a patient, with lichen sclerosus classify the patient as having advanced and severe lichen sclerosus. Though our knowledge of this disease is scares and limited, we know that this diagnosis merits special attention due to the fact the surgical management will be different[10].

Existing literature suggests the lichen sclerosus has a more severe evolution in older patients, and in those that have an increased body mass index. In our study we tried to identify patients that have lichen sclerosus, and we had only 18 patients out of 137 confirmed urethral stricture individuals. But identifying this problem by a simple clinical examination has an important impact in the management of these cases[11,12].

To treat urethral stricture disease in patients with confirmed lichen sclerosus the optimal choice is two stage buccal mucosa graft urethroplasty because it seems that the graft is not affected by the ongoing inflammatory processes related to lichen sclerosus[12].

An attempt to identify risk factors for lichen sclerosus associated urethral stricture is an attempt that has its merits since a more sever evolution of the inflammatory processes associated with LS, might also influence the outcome of any reconstructive urethral surgery[13].

We managed to demonstrate a statistically significant relationship between age of the patient and the severe form LS that might also play a role in the outcome of the undertaken reconstructive surgery.

On the other hand, the relationship between BMI and LS, in our study is not statistically sustainable by results.

Out of the 137 patients only 18 had definitive criteria for clinical diagnosis of LS, and out of these, 17 were circumcised. Our suspicion is that circumcision was performed in these patients in a struggle to treat their lichen sclerosus, and because of secondary effects of LS evolution like phimosis.

We still lack a clear and efficient way to treat LS besides potent topical corticosteroids and other immune modulating drugs like topical applied tacrolimus.

In conclusion urethral stricture disease in combination with LS, has challenges in treating the urethral strictures and they must be taken into consideration when making treatment decision to this regard[14,15].

CONCLUSIONS

Although lichen sclerosus associated urethral stricture has a high association between the presence of lichen sclerosus on one hand, age and body mass index on the other hand, in our study we found only an association between age and lichen sclerosus. Body mass index, had no significantly statistic association with lichen sclerosus in the two subgroups of patients with confirmed urethral stricture disease.

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