

ORIGINAL ARTICLE

Risk factors of urethral diverticula in male patients with spinal cord injury

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Study design: A case-control study in a series of 55 males with urethral diverticula (UD) and their correspondent control, matched by age and time of radiological assessments.

Objectives: To evaluate the risk factors to develop UD in males with spinal cord injury (SCI) and the place in the urethra where they are, most commonly, allocated.

Setting: Toledo, Spain.

Methods: Clinical histories and urodynamic studies, of all patients, were reviewed. The study was completed with a telephone survey according to an established protocol.

Results: The univariate analysis study showed the following risk factors: the age of onset of the spinal injury, the sphincterotomy procedure, personal history of lower urinary tract infections (LUTIs) and the chronic need of either indwelling catheter (IC) or the external condom drainage (ECD). Regarding the location of the UD, we have found the stress urinary incontinence as the only risk factor to develop UD in the prostatic urethra. On the other hand, we can conclude that the sphincterotomy, the ECD, the personal history of LUTIs and the detrusor external sphincter dyssynergia seem to be risk factors to develop diverticula in the bulbo-membranous urethra. Finally, we could point out the IC as the only risk factor for penile UD. Multivariate analysis showed that all of these risk factors were independent among them except the age of the onset of the injury and the ECD for UD in the bulbo-membranous urethra.

Conclusion: According to our study, there is evidence of some specific risk factors for the development of UD in male patients with SCI, and therefore we should adopt the appropriate preventive measures to prevent them.

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INTRODUCTION

Urethral diverticula (UD) constitute an urological pathology most commonly diagnosed in females. They are found in up to 10% of women with lower urinary tract symptoms.¹ However, it becomes a rare pathology in males, except in the group of patients who suffer from spinal cord injury (SCI), where it could be found in up to 4%.^{2,3} According to this prevalence, UD is a common complication in this group of patients, just at the same rate as urinary lithiasis (3.5%). It is even more frequent compared with other SCI complications (renal insufficiency (2.4%), urinary retention (2%) or upper urinary tract infections (0.8%))^{4,5}.

Most UD are asymptomatic, but those that become complicated lead to major disturbances such as calculi, abscesses, periurethral infections, cutaneous fistula and, what is more dangerous, urethral carcinomas.^{6,7}

Most SCI patients develop neurogenic lower urinary tract dysfunction (NLUTD). The aim of a proper management of NLUTD is, mainly, to preserve the renal function and to maintain, as much as possible, the patient's quality of life, by reducing urologic complications.⁸ Therefore, the prevention of UD has a vital importance, and, in order to achieve it, is necessary to become familiar with its risk factors.

There are three main causes of UD: congenital malformation, para-urethral glands infection and the consequences derived from urethral surgery.⁶ Regarding patients with NLUTD, the diverticula are thought to be caused by either indwelling catheter (IC)² or due to sphincterotomy.⁹ However, we have not been able to find, in the literature, any study contrasting these hypotheses.

Our objective is to carry out a case-control study to evaluate clinical and urodynamic risk factors that could be related in the development of UD in male patients with SCI and NLUTD. Moreover, we will investigate whether or not there could be a relation between all these risk factors and the urethral diverticulum allocation.

MATERIALS AND METHODS

A case-control study was performed on a sample group of 55 males with SCI and their correspondent matched controls. The cases were patients who had radiological images showing UD (it had to be an agreement between two radiologists and one urologist). The control group was composed of 55 patients from the same population, without UD, according to the three reviewers.

Clinical history of all patients was thoroughly reviewed. The data were completed by a telephone survey following an established previous protocol, searching for some specific clinical risk factors. Urodynamic studies were also evaluated. All these studies were accomplished according to International Continence Society (ICS) specifications,¹⁰ with a Solar polygraph (MMS, Enschede, The Netherlands).

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The perineal electromyography activity was recorded using anal electrodes. Detrusor external sphincter dyssynergia (DESD) was diagnosed according to the ICS criteria.¹⁰ Stress urinary incontinence (SUI) was defined as the involuntary leakage of urine during increased abdominal pressure, in the absence of a detrusor contraction. The urodynamic diagnosis of bladder outlet obstruction was made according to Bladder Outlet Obstruction Index (BOOI).¹¹

As the study consisted of a retrospective design, specific approval by the ethic committee was not required. However, we asked all patients to sign an informed consent when urodynamic study was performed. Regarding the telephone interview, the answers by the patients were always free.

The program SPSS version 11 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis of the data. The statistical tests used were Fisher's exact test for dichotomous variables, Pearson's χ^2 test for categorical variables and Student's *t*-test comparison of means test for parametric variables. The odds ratio (OR) of each risk factor was calculated with a 95% confidence interval. Finally, a logistic regression analysis was evaluated to determine which variables independently were influencing as risk factors for UD, searching for the maximum coefficient determination and the most parsimonious model. The statistical significance was set on a two-sided 95% level. The quantitative variables were expressed as mean \pm s.d.

RESULTS

Descriptive statistics

Patients' mean age was 45 ± 12.2 years, and the mean time course of the lesion was 203 ± 124.1 months. The level and grade of spinal injury are shown in Table 1.

The medical treatments that the patients received were anticholinergic drugs in 60 cases (54.5%), alpha-adrenergic blockers in 6 cases (5.5%), anticholinergics and alpha-blockers in 2 cases (1.8%) and no treatment in 40 cases (36.4%). These data were not registered in 2 cases (1.8%).

Regarding the surgical personal background, we found that no surgical procedures were performed in 80 cases (72.7%).

On the other 27.3% of the patients there were a significant variety of surgical treatments. Sphincterotomy was carried out in 17 cases (15.4%) and some other urethral procedures in 6 cases (5.4%), 3 cases of bladder operation (2.7%) and 2 more cases (1.8%) of scrotal surgery.

Regarding renal procedures, we found 3 cases (2.7%) of renal lithotripsy, 3 cases (2.7%) of endoscopic treatments for vesicourethral reflux and 1 case (0.9%) of a combination of urethral plus an endoscopic procedure for vesicoureteral reflux.

In relation to the different types of catheters, an overall of 48 patients (43.6%) were under clean intermittent catheterization (CIC), 30 patients (27.3%) carried indwelling catheter (IC) and 65 patients (59.0%) used external condom drainage (ECD). There was one patient (0.9%) who had a cystostomy.

The mean number of urinary infections was 1.1 ± 2.27 infections per year. We found them in the lower urinary tract (cystitis) in 30 cases (27.3%), affecting the testes and epididymitis in 5 cases (4.5%).

They were diagnosed as pyelonephritis in 7 cases (6.4%), orchiepididymitis and pyelonephritis together in just 1 case (0.9%) and they had an unknown origin in 5 cases (4.5%). In 63 patients (57.3%), there weren't any urinary infections.

Urodynamic study was carried out in all cases. Neurogenic detrusor overactivity (NDO) was shown to happen in 91 patients (82.7%), whereas a detrusor external sphincter dyssynergia (DESD) was demonstrated in 87 patients (79.1%). The bladder outlet obstruction was shown in 41 cases (37.3%). The stress urinary incontinence (SUI) could be demonstrated to happen in 10 patients (9.1%), and, finally, a detrusor areflexia (detrusor acontractile) was found in 16 cases (14.5%).

Inferential statistics

Risk factors for UD. The number of patients with diverticula according to the level of SCI are the following: Between C4–C6: 22 patients (51%), between D1–D6: 11 patients (30%), between D7–L2: 19 patients (49%) and between L3–cauda equina: 3 patients (50%).

The clinical parameters that our study has been able to demonstrate as a risk factor for UD were the following: the age of SCI: 239 ± 131.4 months in patients with UD versus 168 ± 106.2 months in patients without UD ($P=0.000$). The sphincterotomy procedure had been carried out in 14 patients (25.5%) with UD versus 3 patients (5.5%) without UD ($P=0.002$). We conclude that the OR to develop UD after a sphincterotomy procedure is 5.89 times more than if the patient has not had this operation previously (confidence interval between 1.9 and 1.8).

A total of 21 patients (38.2%) with UD had indwelling catheter versus 9 patients (16.4%) without UD ($P=0.008$). OR: 3.14 (confidence interval between 7.15 and 3.12). A total of 38 patients (69.1%) with UD had ECD versus 27 patients (49.3%) without UD ($P=0.031$). OR: 2.30 (confidence interval between 4.47 and 1.18). A total of 21 patients (38.0%) with UD had lower urinary tract infections (LUTIs) versus 9 patients (17.1%) without UD ($P=0.0369$; OR: 2.96; confidence interval between 6.89 and 1.27).

None of the urodynamic parameters could be found to represent a risk factor for UD.

Risk factors for diverticula located in prostatic urethra. Our study concluded that none of the clinical parameters showed to be risk factors for UD when situated in prostatic urethra.

On the other hand, there was just only one urodynamic parameter that could be called risk factor: the SUI. Patients with prostatic UD had SUI in 4 cases (40%) versus 6 patients (4.3%) without prostatic UD ($P=0.003$).

Risk factors for diverticula in bulbo-membranous urethra. Patients who presented bulbo-membranous UD had undergone sphincterotomy in 10 cases (30.2%) versus 4 cases (5.9%) of patients without bulbo-membranous UD ($P=0.000$). Patients with bulbo-membranous UD carried ECD in 31 cases (72.1%) versus 34 patients (50.6%) without bulbo-membranous UD ($P=0.024$). Moreover, patients with bulbo-membranous UD had LUTIs in 18 cases (42.1%) versus 12 patients (18.3%) without bulbo-membranous UD ($P=0.014$). The rest of the clinical parameters did not show statistical significant differences.

The only urodynamic parameter that showed to be a risk factor was the DESD. Patients with diverticula in bulbo-membranous urethra had DESD in 41 cases (94.7%) versus 48 patients (71.2%) without bulbo-membranous UD ($P=0.004$).

Risk factors for diverticula in penile urethra. Regarding the UD located in the penile urethra, our study did find just one clinical parameter

Table 1 Level and grade of spinal cord injury

Grade of injury	Level of injury				Total
	C4-C8	D1-D6	D7-L2	L3-cauda equina	
Incomplete	16	6	9	6	37
Complete	21	22	29	1	73
Total	37	28	38	7	110

statistically significant. It was the presence of indwelling catheter. Patients with penile UD had indwelling catheter in 11 cases (45%) versus 19 patients (22.2%) without penile UD ($P=0.049$).

Focusing on the urodynamic parameters, we could find just only one significant, which was the presence of DESD. Patients with penile UD had DESD in 16 cases (61.1%) versus 73 patients (83.7%) without penile UD ($P=0.004$).

Multivariate analysis. Multivariate analysis showed that the independent risk factors for UD were the history of sphincterotomy, LUTI, to carry indwelling catheter and to have ECD.

The independent risk factors for the presence of UD in bulbo-membranous urethra were the history of sphincterotomy and the DESD and regarding the penile urethra was the indwelling catheter and the DESD.

DISCUSSION

Our study clearly demonstrates that the LUTIs, IC, the ECD and the sphincterotomy are all independent risk factors to develop UD.

LUTIs are one of the most frequent urologic complications in patients with SCI.⁵ LUTIs were significantly more frequent in patients with UD than the control group (38% versus 17%). The raw OR to develop UD, in the presence of LUTI, is 2.96 and 2.44 controlling the rest of variables by multivariate analysis. The prevalence of LUTIs in patients with UD that is located in bulbo-membranous urethra was also higher than in any other urethral locations.

Urinary infections are one of the etiological mechanisms proposed to explain the UD formation. It is supposed that the mechanism for which LUTIs develop UD in women could be explained by infected para-urethral glands that get obstructed, and, later in time, the abscess would break itself into the urethral lumen^{5,6} resting a UD. There has been described UD in males associated with infectious process, urethral suppuration¹² and prostatitis¹³ as well. This process has been also described in SCI patients with recurrent LUTI.¹⁴

Bladder evacuation management is vital in patients with SCI in order to reach continence, prevent recurrent urinary tract infection and maintain the renal function. There are basically three options to achieve this goal: a clean intermittent catheterization; reflex or straight voiding, with or without ECD and, finally, the arrangement of IC (transurethral or suprapubic).¹⁵

IC has been demonstrated to be a serious risk factor for developing UD. Patients with UD were subject to IC in more proportion (38%) than the patients without UD (16.4%). The raw OR is equal to 3.14. Moreover, this kind of bladder evacuation was more frequent in patients with penile UD (45% versus 22%). The association between IC and UD in SCI patients was already stated in other studies.³ Ronzoni *et al.*⁷ published a series in which they showed that the total amount of patients who suffered from a relapsed UD after surgical treatment had carried an IC.

IC is a very well known risk factor for urinary infection in patients with SCI. A medical study carried out in our Centre demonstrated that the risk to present an urinary infection in males with IC was up to four times more frequent.¹⁶ However, multivariate analysis shows that IC is independent for LUTIs as UD risk factor. This analysis increases the risk of UD from a raw OR of 3.1 to 12.87 controlling the rest of the variables. These data confirm us the strong correlation between LUTIs and IC. On the other hand, it has been observed that the presence of IC supposes the highest risk to develop UD compared with all the analysed risk factors. The main mechanism why IC causes UD would be different from LUTIs. It was suggested that a certain mechanical

effect was exerted directly on the urethra, due to compression, consequently causing ischemia of the urethral mucosa.¹⁷

ECD is also an alternative choice to IC that can be used, in males, with urinary incontinence.¹⁸ The incidence of bacteriuria and symptomatic urinary tract infections is much lower in patients with ECD than in those with indwelling catheter.¹⁶ However, we have observed that ECD constitutes, as well, a risk factor for UD. The raw risk for UD of patients with ECD was 2.3 times more. This risk increases to 6.31 after controlling the rest of the predictive variables. Moreover, patients with UD located in bulbo-membranous urethra had ECD more frequently than the rest of the patients (72.1% versus 50.6%).

ECD would cause UD by a different mechanism than LUTIs, because patients with ECD show the same incidence of LUTIs as clean intermittent catheterization's patients.¹⁶ The effect would be promoted by compression of urethra. Golji *et al.*¹⁹ had already observed the presence of cutaneous lesions and UD formations in patients with ECD.

In our study, we have found that the sphincterotomy is an important risk factor for UD with a raw OR of 5.89, which descends to 3.69 when controlling the rest of the predictive variables. Sphincterotomy was also more frequent in patients with bulbo-membranous diverticula. Urethral surgical procedures are known as risk factors of UD in males. Juma *et al.*⁹ described in 1995 the appearance of three cases of UD after sphincterotomy. Our study has been able to confirm and quantify such risk.

SUI takes place in NLUTD, especially because of a lesion in the pudendal cord centre, and it could also be due to sphincterotomy after having treated a case of DESD.²⁰ An association between SUI and UD in females has been shown,¹ although there is no proven cause effect relationship mainly because there are only transversal studies in the literature.

In a former work,²¹ we hypothesized that traumatic catheterization could favor UD. This would imply that the antecedent of clean intermittent catheterisms would be more frequent in patients with bulbo-membranous UD. Unfortunately, our data did not confirm that hypothesis.

In our study, DESD constituted also a risk factor for UD in bulbo-membranous urethra, whereas it was significantly less frequent in those diverticula located in the penile urethra. This risk factor was independent of sphincterotomy. In this case, the mechanism of development could be related to maintain contraction of external sphincter, which can produce UD at this level.

We are aware of several limitations in our study. The most representative one is the retrospective data collection. We have tried to avoid this limitation by making a telephonic survey to the patients.

The other limitation would consist on the selection of a control group. We have strongly tried to match the controls with cases based on the date of radiologic study and age group, but we assume that there could be some selection bias. The diagnosis of UD based on radiological studies is difficult, and therefore we have used the agreement of three independent explorers.

In spite of these limitations, we can affirm, as far as we are aware, that this is the first non-descriptive study regarding the risk factors for developing UD in SCI patients.

Finally, our study confirms and quantifies several risk factors that surely influence in the appearance of UD in males with SCI. Consequently, measures to avoid its appearance should be adopted.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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