Contemporary Urethral Stricture Characteristics in the Developed World

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OBJECTIVE To assess the current etiology, features, and natural history of urethral stricture disease in the developed world.

MATERIALS AND METHODS We analyzed the data from 1439 male patients with urethral stricture, who had undergone surgical treatment in our referral urethral center from 2000 to 2010. The preoperative evaluation included a detailed clinical history of stricture, uroflowmetry, retrograde and voiding cystourethrography, and urethroscopy. Statistical analysis was done for the stricture site, length, and etiology, patient age, and previous treatments.

RESULTS Strictures were posterior in 112 (7.8%) and anterior in 1327 (92.2%). In the anterior group, 439 were penile (30.5%), 675 bulbar (46.9%), 71 penile plus bulbar (9.9%), and 142 panurethral (4.9%). The main causes were iatrogenic in 556 (38.6%), unknown in 515 (35.8%), lichen sclerosus in 193 (13.4%), and trauma in 156 (10.8%). The main iatrogenic strictures were from catheterization in 234 (16.3%), hypospadias repair in 176 (12.2%), and transurethral surgery in 131 (9.1%). The stricture distribution increased until about 45 years and then decreased. Strictures were uncommon in those <20 and >70 years old. The mean length was 4.15 cm; longer strictures were found in those with lichen sclerosus (7.45 cm) or after hypospadias repair (4.42 cm) and catheterization (4.40 cm). The mean length was also greater in the pretreated (4.34 cm) than in the untreated (3.64 cm) strictures.

CONCLUSION Urethral stricture in developed countries mainly involves the anterior urethra, in particular the bulbar tract. The most common cause was iatrogenic. Hypospadias repair and lichen sclerosus represent emerging important causes. Finally, urethral stricture is not a disease of the elderly but involves all ages. UROLOGY 81: 191–197, 2013. © 2013 Elsevier Inc.

Male urethral stricture is one of the oldest and most difficult diseases known in urology. It has the potential for a significant economic impact and burden on each patient and the society as a whole.[1] Nevertheless, a detailed assessment of this pathologic entity is still lacking. This is because the urethra is a complex organ, characterized by different areas, each of which is prone to stricture of different types. Furthermore, in the past few decades, its clinical history seems to have changed. Moreover, the differences between the developed and developing countries should be considered.

The published data contain few studies concerning the stricture etiology, with most information reported only in relation to the description of various reconstructive techniques.[2-4] Only 2 recent publications have focused on the specific topic of etiology but with small series of patients.[5,6]

Many questions about the characteristics of urethral strictures are still waiting additional study. These questions included the main causes of stricture today, the prevalence of the different causes, how strictures from different sites differ in terms of etiology, length, or patient age, which ages are most affected by the disease, and whether previous treatments worsen the stricture. The answers to these questions could help prevent the development or worsening of the processes that cause the strictures.

We evaluated a large series of patients with urethral stricture to discover new information, in an effort to better understand the features and natural history of this complex urologic disease in a developed country.

MATERIAL AND METHODS

A retrospective study was performed in our Italian referral center for urethral reconstruction to analyze the whole database of male patients with urethral stricture who had undergone surgical treatment from 2000 to 2010, regardless of age.

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A total of 1439 patients were diagnosed, evaluated, and surgically treated by the same urologist (E.P.). The preoperative evaluation included a detailed clinical history of the urethral stricture disease, physical examination, uroflowmetry, retrograde and voiding cystourethrography, and urethroscopy.

With regard to the anatomic differences, we classified the strictures as posterior or anterior, with the latter further divided into 4 subgroups: penile, bulbar, panurethral (long and uninterrupted penobulbar strictures), and penile plus bulbar (interrupted and concomitant strictures in these urethral segments).

According to the published data, the etiology was classified as unknown, congenital, infection, trauma, iatrogenic, lichen sclerosus (LS), and tumor.[2,5-8] The iatrogenic subgroup included strictures subsequent to urologic procedures involving the urethra, including transurethral surgery (TS), prostate adenomectomy, prostatectomy, radiotherapy, hypospadias repair (HR), and catheterization. Strictures were classified as resulting from catheterization when urethral catheter insertion was the only urethral manipulation that had occurred. In many patients, the catheterization had been performed a long time before the stricture diagnosis or in an anesthetized, sedated, or confused patient. Therefore, exact data for the reason of catheterization, exact duration and catheter type, and whether the catheterization was traumatic were lacking. In the strictures classified as resulting from LS, LS had been pathologically confirmed by biopsy findings.

Statistical Analysis

Statistical analysis was performed using the SPSS, version 12.0, software. Differences between groups for quantitative variables and differences in the distribution of categorical variables were tested with 1-way analysis of variance and the chi-square test, respectively. Data are presented as the mean ± standard deviation. An α of 5% was considered the threshold for significance.

RESULTS

Of the 1439 patients, 1402 (97.4%) underwent urethroplasty and 37 (2.6%) internal urethrotomy. The main characteristics of the study data set are listed in Table 1.

Stricture Site

Of the 1439 patients, 112 (7.8%) presented with a posterior urethral stricture and 1327 (92.2%) with an anterior urethral stricture. In the anterior stricture group, the urethral site was penile in 439 (30.5%), bulbar in 675 (46.9%), panurethral in 142 (9.9%), and penile plus bulbar in 71 (4.9%).

Etiology

We identified several causes of stricture. Most were iatrogenic (556 [38.6%]) or unknown (515 [35.8%]). LS was the etiology in 193 cases (13.5%) and trauma in 156 (10.8%). Of the iatrogenic cases, the most frequent causes were catheterization in 234 cases (16.3%), HR in 176 (12.2%), and TS in 131 (9.1%).

In the penile urethral strictures, the main causes were HR in 140 cases (31.9%), LS in 107 (24.4%), and catheterization in 71 (16.2%). In the bulbar urethral strictures, the etiology was unknown in 417 (61.8%), catheterization in 117 (17.3%), and TS in 59 (8.7%). In

Table 1. Urethral stricture characteristics

	Site					
Variable	Penile (n = 439; 30.5%)	Bulbar (n = 675; 46.9%)	Panurethral (n = 142; 9.9%)	Penile Plus Bulbar (n = 71; 4.9%)	Posterior (n = 112; 7.8%)	Total (n = 1439)
Mean age (y)	45.2 ± 17	42.2 ± 16.3	55.6 ± 13.4	47.4 ± 14.5	47.2 ± 18.6	45.1 ± 6.9
Mean length (cm)	3.65 ± 2.4	2.83 ± 1.4	12.19 ± 2.8	6.51 ± 2.8	2.45 ± 1.7	4.15 ± 3.4
Etiology						
Unknown	56 (12.7)	417 (61.8)	32 (22.5)	7 (9.9)	3 (2.7)	515 (35.8)
Trauma	10 (2.3)	59 (8.8)	0	6 (8.5)	81 (72.3)	156 (10.8)
LS	107 (24.4)	0	69 (48.6)	17 (23.9)	0	193 (13.5)
Other*	12 (2.7)	5 (0.7)	1 (0.7)	1 (1.4)	0	19 (1.3)
Iatrogenic	254 (57.9)	194 (28.7)	40 (28.2)	40 (56.3)	28 (25.0)	556 (38.6)
Iatrogenic subgroup						
Catheterization	71/234 (30.4)	117/234 (50)	23/234 (9.8)	20/234 (8.5)	3/234 (1.3)	234/556 (42.1)
TS	43/131 (32.9)	59/131 (45)	10/131 (7.6)	8/131 (6.1)	11/131 (8.4)	131/556 (23.6)
HR	140/176 (79.6)	17/176 (9.6)	7/176 (4)	12/176 (6.8)	0	176/556 31.6()
Other†	0	1/15 (7)	0	0	14/15 (93)	15/556 (2.7)
Previous treatment	349 (79.5)	497 (73.6)	110 (77.5)	58 (81.7)	46 (41.1)	1060 (73.7)

HR, hypospadias repair; LS, lichen sclerosus; TS, transurethral surgery.
Data presented as mean ± standard deviation or n (%).
* Congenital, infection, tumor.
† Radiotherapy, prostate adenomectomy, prostatectomy.

the panurethral site, the etiology was LS in 69 (48.6%), unknown in 32 (22.5%), and catheterization in 23 (16.3%). The main cause of the penile plus bulbar multifocal strictures were catheterization in 20 (28.2%), LS in 17 (23.9%), and HR in 12 (16.8%). In the posterior urethra, TS was a minor cause (n = 11; 9.8%), and the main cause was pelvic trauma (n = 81; 72.3%); the stenoses from the latter category are commonly denominated in published studies as "pelvic fracture urethral distraction defects."

Other minor causes of strictures included congenital in 10 (0.7%), infection in 7 (0.4%), tumor in 3 (0.2%), and in the "other" category of the iatrogenic group, radiotherapy in 1 (0.1%), prostate adenomectomy in 5 (0.3%), and prostatectomy in 9 (0.6%).

Patient Age

The mean patient age was 45.1 ± 16.1 years (range 2-84). Patients with bulbar strictures were significantly younger than those in all other groups ($P = .001$; Table 1). The frequency of strictures tended to increase until about 45 years (median value) and then decreased. The development of strictures was more frequent between 20 and 70 years of age and were uncommon outside this range (Fig. 1).

In the 0-10 year age group, the strictures were mainly localized in the penile urethra, and in the 11-40 year group, in the bulbar urethra. In those >41 years old, the strictures were uniformly localized in the penile and bulbar urethra. The panurethral strictures were more frequent in patients >51 years (Fig. 1A).

The main cause of stricture was iatrogenic (particularly HR) in the 0-20 year group, unknown in the 21-50 year group, and iatrogenic in those >51 years (Fig. 1B). Patients with urethral strictures related to previous transurethral surgery were significantly older than those in the other groups ($P = .001$; Table 2).

Stricture Length

When stratified by the different stricture etiologies, urethral strictures secondary to LS were significantly longer than those from the other etiologies ($P = .001$; Table 2).

Most of the pretreated strictures were from unknown causes (383 [36.1%]), catheterization (177 [16.7%]), HR (159 [15%]), and LS (144 [13.6%]).

Previous Treatment

Of 1439 patients enrolled in our study, 1060 (73.6%) had received previous treatments at other centers, and 379 (26.4%) were evaluated for the first time by our group (Table 3). The patients who had received previous treatments were significantly older and presented with longer strictures than the patients treated for the first time by our group ($P = .001$).

Overall, the mean urethral length was 4.15 ± 3.4 cm. The panurethral strictures (12.19 ± 2.8 cm) were significantly longer than in the other groups of urethral strictures ($P = .001$; Table 1).

COMMENT

Most Common Stricture Site

Our findings have confirmed that urethral stricture in developed countries mainly involves the anterior urethra (92.2%), in particular, the bulbar tract (46.9%), with the posterior urethra involved only in 7.8% of cases.[5,6,8] This explains why general urologists manage mainly bulbar strictures and, more rarely, penile strictures. The rarest posterior strictures are treated in highly specialized centers.[7]

Current Most Common Stricture Etiology

Past reports on stricture etiology have been characterized by small series of patients. They have shown that in the past few decades, among the male population of developed nations, a reduction of inflammatory causes has occurred with an increase in iatrogenic and unknown causes, although in the developing nations, the main causes are traumatic and inflammatory.[2,5,9]

Our large series has proved that the main cause of strictures is iatrogenic (38.6%): mostly catheterization (16.3%) and TS (9.1%). Thus, urologists should be particularly careful when handling the urethra to reduce the trauma that could cause future stricture formation.[5,10,11] The data that a certain percentage of stenoses are catheter induced might lead to the suggestion of a restriction on the indications for potentially harmful catheterizations, the avoidance of needless catheterizations, and, if necessary, the use of small catheters for short durations or suprapubic cystotomy when prolonged urinary drainage is required. However, several investigators have supposed that the urethral ischemia, activating the stenosing spongiofibrosis, might be caused by the combination of an indwelling catheter with a reduced local blood flow in hypovolemic states, such as in open heart surgery or similar hemodynamic situations. This pathogenesis was considered responsible for urethral stricture formation in a relevant number of patients undergoing cardiosurgery. Consequently, these investigators suggested the use of suprapubic cystostomy, instead of an urethral catheter, because the latter increases urethral ischemia.[12-14]

Iatrogenic strictures subsequent to HR represented 12.2% of the cases; therefore, pediatric surgeons should inform parents that children undergoing HR could develop strictures in the future and should be monitored for stricture formation. These data seem to confirm that HR has a high rate of complications, of which we only know the bare minimum. In particular, of 176 patients with HR strictures, 34 (19.3%) had an association with LS, making treatment even more difficult to manage.

Few radiation-induced strictures were encountered than we would have expected for a developed country, although this finding was consistent with the published data.[5]

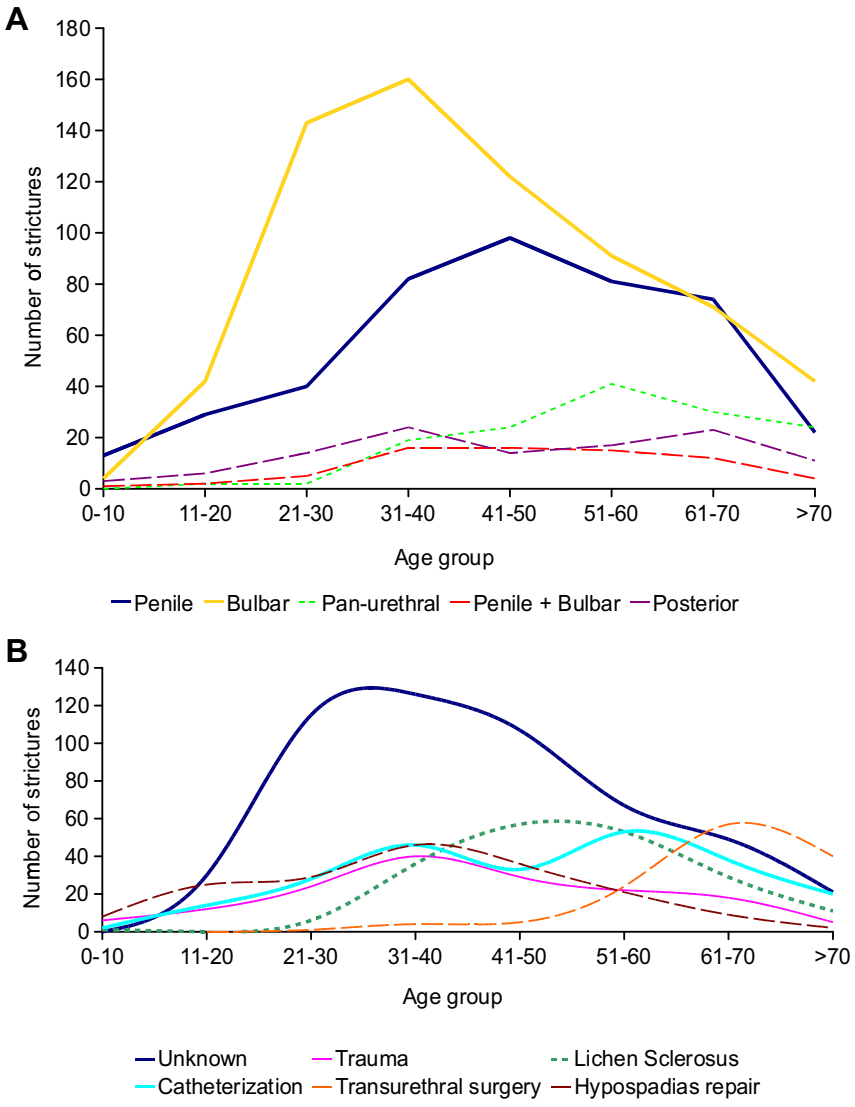

Figure 1. Age distribution of **(A)** stricture site and **(B)** stricture etiology across age groups. (Color version available online.)

Table 2. Urethral strictures characteristics according to etiology

Etiology	Patients (n)	Mean Length (cm)	Mean Age (y)	Previous Treatment (n = 1060; 73.6%)
Unknown	515	3.40 ± 2.7	41.2 ± 15.3	383 (36.1)
Trauma	156	2.54 ± 1.3	40.9 ± 16.3	67 (6.3)
LS	193	7.45 ± 4.9	50.3 ± 12.5	144 (13.6)
Iatrogenic		4.21 ± 3.6	48.3 ± 15.5	459 (43.3)
Iatrogenic subgroups				
Catheterization	234	4.40 ± 3.6	47.5 ± 15.5	177 (16.7)
TS	131	3.87 ± 3.1	64.7 ± 10	111 (10.5)
HR	176	4.42 ± 3	35.6 ± 15	159 (15.0)

Abbreviations as in Table 1.
Data presented as mean ± standard deviation or n (%).

A large part (35.8%) of our strictures were of unknown etiology, especially in the bulbar tract; perhaps some of these strictures had been caused by unrecognized childhood perineal trauma or were congenital.[15] Another explanation could be inflammation from "undetected" infections that lie in the Littre glands located mainly in the mid/proximal bulb.[8,16] However, we observed that the "detected" infectious causes (0.4%) had considerably decreased, probably thanks to the widespread use of condoms in developed countries. Regardless, experts should make an effort to clarify this large group of unknown bulbar strictures.

Table 3. Previous treatment by mean age, mean length, and stricture site

	Patients (n)	Mean Age (y)	Mean Length (cm)	Site				
				Penile	Bulbar	Panurethral	Penile Plus Bulbar	Posterior
No previous treatment	379 (26.4)	41.5 ± 16.4	3.64 ± 3.3	90 (20.5)	178 (26.4)	32 (22.5)	13 (18.3)	66 (58.9)
Previous treatment	1060 (73.6)	46.4 ± 16.4	4.34 ± 3.4	349 (79.5)	497 (73.6)	110 (77.5)	58 (81.7)	46 (41.1)
Dilation	114 (7.9)	49.8 ± 17.3	5.30 ± 4.2	48 (10.9)	30 (4.4)	23 (16.2)	8 (11.3)	5 (4.4)
Urethrotomy	334 (23.2)	42.8 ± 16.6	3.46 ± 2.5	49 (11.2)	240 (35.6)	16 (11.3)	10 (14.1)	19 (17.0)
Urethroplasty	147 (10.2)	41.3 ± 17.1	4.89 ± 3.9	98 (22.3)	18 (2.7)	11 (7.7)	13 (18.3)	7 (6.3)
Stent	3 (0.2)	43.3 ± 9	3.33 ± 1.5	0	3 (0.4)	0	0	0
Multiple	462 (32.1)	49.7 ± 15.9	4.57 ± 3.5	154 (35.1)	206 (30.5)	60 (42.3)	27 (38.0)	15 (13.4)

In Western countries today, the most common cause for inflammatory strictures is LS. The virtual increase of this dermatologic-urologic pathologic entity has probably resulted from its relatively recent identification and classification as a cause of urethral disease. However, the incidence of urethral involvement in male patients with genital LS and the percentage of LS strictures of the total number of strictures remains unknown. In our series, it was 13.5%. In particular, it was the main cause (48.6%) of long panurethral strictures and the second cause (24.4%) of penile strictures, after HR. LS progressively affects the prepuce, glans, and meatus. Meatal stenosis leads to high-pressure voiding and inflammation of the periurethral glands, with potential progressive panurethral involvement.[8,17] This would explain why we have never observed a single bulbar stricture in association with LS without involvement of the distal urethra. Furthermore, intervention on a meatal or penile stricture in the early stages of the disease, instead of useless dilation, could be useful in stopping the large diffusion of urethral involvement. Another interesting observation was that we did not find LS in the posterior urethra, in accordance with the theory that the disease does not involve the different epithelium of this tract. These data confirm the need for additional study of this disease to understand the etiopathogenetic processes and find appropriate treatment.

Trauma was a recognized cause in 10.8% (5.6% of anterior and 72.3% of posterior strictures, respectively), in contrast to the greater incidence of ≤31% for traumatic strictures in developing countries with poor traffic regulations.[18]

Despite the high number of pretreated patients and those with a long history of stricture, tumor was present in only 0.2% of cases. However, the published data have not confirmed the assumption that the prolonged state of inflammation of stenotic tissues and repeated traumatic procedures (eg, dilations) could increase the risk of developing urethral cancer.

Urethral Stricture: A Disease of All Ages

The strictures were frequent in those aged 20-70 years and rare outside this range, in contrast to the belief that the incidence of stricture increases proportionally with the age, especially in patients >55 years.[8] Thus, urethral stricture is not a typical disease of the elderly but involves all ages, with a potential effect on the patient's sexual activity and quality of life and with social costs.

When stratified by site and age group (Fig. 1A), the strictures were mainly localized in the penile urethra in those <10 years and in the bulbar urethra in those aged 11-40 years. In those >41 years, they were uniformly localized in the penile and bulbar urethra. Most of the long panurethral strictures were present in patients >51 years (mean 55.6). When stratified by stricture etiology and age group (Fig. 1B), the stricture etiology was mainly iatrogenic (in particular, HR) in those <20 years, unknown in those aged 21-50 years, and, again, iatrogenic (mainly catheterization and TS) in those >51 years.

The Longest Strictures

In our series, the mean length was greatest for panurethral (12.19 cm) and LS (7.45 cm) strictures. The length of the strictures was greater in the pretreated patients (mean 4.34 cm) than in the untreated ones (mean 3.64 cm). The mean stricture length was greater (5.30 cm) and the mean patient age (49.8 years) was older in the patients undergoing dilation. These data are in agreement with the previous assumption that elderly men with a history of previous instrumentation develop longer strictures than younger and untreated men. All this suggests that inappropriate and repeated procedures (ie, internal urethrotomy and dilation) could potentially transform a simple and short stenosis in a longer and more complex stricture.[19] Because most of the patients referred to our center had undergone repeated dilation and/or internal urethrotomy, our study has confirmed the existence of a trend among urologists, who initially resort to minimally invasive procedures, instead of opting for urethroplasty as the first choice procedure. More penile urethroplasties were performed before referral to our center than bulbar urethroplasties. This might have been because penile urethroplasties are more difficult to perform and prone to failure considering the scarcity of spongious tissue. In contrast, bulbar urethral repairs are more amenable to

anastomotic urethroplasty, easier to perform, and less prone to failure because of the abundant spongiosum available.

Finally, we believe that considering stenoses from a length/site standpoint only and as idiopathic for the most part are outdated concepts. In our study, we investigated the actual percentage of the emerging causes of stenosis in the largest series of patients ever analyzed. These demographic data might help to prevent the development or worsening of urethral stricture disease and might help the experts to determine the most adequate therapeutic strategy. However, the limitation of our study was that the results might not accurately reflect all patients with urethral stricture disease, but rather describe only those patients with disease severe enough to require surgery at a referral reconstructive center.

CONCLUSION

Our findings have shown that urethral stricture in developed countries mainly involves the anterior urethra, in particular, the bulbar tract. The most common cause of stricture formation was iatrogenic; thus, particular care must be taken when handling the urethra. HR and LS represented important emerging causes, responsible for most penile and panurethral strictures, which are also commonly acknowledged as the most difficult to treat. Finally, urethral stricture is not a disease of the elderly but involves all age groups.

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EDITORIAL COMMENT

The authors present a 10-year retrospective case series of Italian patients with urethral stricture disease. The report is a descriptive analysis of 1439 patients with anterior or posterior urethral strictures who presented to a single reconstructive referral center and single surgeon. The aim of their report was to examine the preoperative demographics of the patient cohort with the known exposure of a urethral stricture. No mention is made of whether the patients were recruited consecutively; however, they did not describe any exclusion criteria to indicate otherwise. Finally, LS-related strictures were pathologically confirmed to provide confirmation of the presumptive diagnosis.

The authors present important reconstructive questions in their first paragraphs regarding the preoperative demographics of patients with urethral strictures in the modern era. From their single-site data, they answered these reconstructive questions. However, practitioners in other parts of the world, developed and undeveloped, cannot generalize these data to answer the proposed reconstructive questions provided in the authors' report; however, their study is interesting and relevant. Furthermore, this single-center case series is an important first step toward possible future studies of broadened scope.

Several points deserve mention. First, most patients had received previous urologic care for their strictures (73.6%), and, not surprisingly, this cohort of patients had significantly longer strictures than patients who had never been previously treated for their urethral stricture (previous treatment 4.34 cm vs no previous treatment 3.64 cm). Next, after stratification by etiology, LS-related strictures were the longest strictures (7.45 cm). As such, minimally invasive methods to definitively treat these complex strictures should not be considered. Finally, among their cohort of Italian men who had undergone previous treatment, urethral dilations tended to be used for penile, panurethral, or penile plus bulbar strictures (69%), and urethrotomy tended to be used for bulbar strictures (72%, their Table 3). From this finding, it was not surprising that urethral strictures tended to be the longest among the previously treated patients who had undergone previous dilation.

The authors should be congratulated for their descriptive analysis of the preoperative demographics from their reconstructive referral center. The data are clinically useful and

provide useful insight regarding the modern, preoperative demographics of urethral strictures.

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REPLY

Our study, with a large consecutive series of patients with urethral stricture disease (USD), highlighted some interesting relevant points useful in the prevention of the worsening of the disease that could be of help for the specialists who treat these patients.

In the first place, we ascertained that, in contrast to the traditional belief, USD is not a typical pathologic feature of the elderly but involves all ages (mean age 45 years), with a potential effect on patients' sexual activity and quality of life and presenting with a social cost. Thus, the disease and the outcomes of its treatment also need to be assessed from a sexual viewpoint, not just with regard to urinary function.[1]

The most common cause of strictures was iatrogenic; consequently, particular care must be taken by urologists when handling the urethra. We need studies to define the real percentage of USD risk after different types of urethral manipulation (ie, catheter, endoscopy, transurethral surgery), because it could be important for correct urologic counseling of patients who must undergo these procedures.

HR and LS represent important emerging causes of strictures that are very difficult to treat. Surgeons treating patients affected by these pathologic entities need a particular surgical expertise that general urologists usually do not possess. Thus, it would be advisable to manage these complex pathologic entities at referral centers.

All these considerations and others (eg, the damaging effect of useless repeated dilation and urethrotomy) highlight the need for a change in the previous philosophy concerning the treatment of USD, which, unfortunately, is hard to extinguish.[2]

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