



Urethral Stricture is Frequently a Morbid Condition: Incidence and Factors Associated With Complications Related to Urethral Stricture

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OBJECTIVE	To determine the frequency of complications related to urethral stricture and identify clinical factors associated with them.
METHODS	Of 1851 patients with a suspected diagnosis of urethral stricture referred to a single urologist from 2005 to 2016 were retrospectively reviewed. Clinical variables included complications directly related to urethral stricture at the time of patient presentation, associated signs/symptoms, patient age, stricture length, location, and etiology. Complications considered significant were acute urinary retention or difficult catheterization requiring emergent urologic intervention or renal failure, urosepsis, or urethral abscess directly related to stricture. Patients without complete data were excluded from study. The occurrence of complications was compared in relation to patient age, symptoms, stricture length, location, and etiology using binary logistic regression.
RESULTS	Of 1023 patients meeting inclusion criteria, mean age was 48.0 years and mean stricture length was 5.0 cm (1-18). Of 40.6% (415) of patients experienced at least one complication directly related to urethral stricture including acute urinary retention (32.6%), difficult catheterization (16.0%), urethral abscess/urosepsis (5.0%), or renal failure (3.1%). On multivariate analysis, stricture length (cm) (odds ratio [OR] 1.1; 95% confidence interval [CI] 1.1-1.2, $P = .01$), lack of reported lower urinary tract symptoms (OR 3.8, 95%CI 1.9-7.3, $P < .0001$), posterior stenosis (OR 3.0, 95%CI 1.3-6.8, $P = .01$), and trauma-related strictures (OR 1.6, 95% CI 1.1-2.4, $P = .02$) were associated with complications. Lastly, 7.0% of patients experienced complications deemed to be life-threatening.
CONCLUSION	Urethral stricture is frequently a morbid condition. Patients with longer strictures, posterior stenoses, absence of preceding lower urinary tract symptoms and traumatic strictures are at highest risk for complications related to urethral stricture and should likely be directed toward more definitive treatment. UROLOGY 132: 189–194, 2019. © 2019 Elsevier Inc.

Urethral stricture is fundamentally a fibrosis of the urethral epithelial tissue and corpus spongiosum that in turn causes stenosis of the urethral lumen.¹ As the urethral lumen progressively narrows, varying degrees of obstruction occur. Most of the symptoms related to urethral stricture are thought to be directly related to this decrease in urethral caliber.¹ Typical symptoms include lower urinary tract symptoms (LUTS) such as weak urinary stream, straining to void, urinary hesitancy, incomplete

emptying, nocturia, and frequency.² Other signs and symptoms such as genitourinary pain, urinary tract infection, ejaculatory dysfunction, urethral discharge, and hematuria may also occur.³ The prevailing mindset is that urethral stricture adversely impacts voiding function and quality of life but it is unclear how it impacts overall health status.^{4,5} When complications occur, at least in developed nations, they are often thought to be minor.⁵ It is widely thought that more severe complications are experienced by only a small minority of men especially in the modern era.⁶⁻⁸ However, this assumption remains largely untested and it is entirely possible that a substantial proportion of patients with urethral stricture will experience significant complications requiring emergent urologic care including renal failure, urethral abscess, acute urinary retention, and difficult catheterization even in a contemporary population of

Source of funding: None.

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Submitted: April 23, 2019, accepted (with revisions): July 11, 2019

patients living in an industrialized nation.³ Additionally, some of these complications can be considered life-threatening. For example, urethral stricture is a known but poorly quantified risk factor for Fournier's gangrene.⁹

The objective of this study is to determine the incidence of significant complications related to urethral stricture and to identify which clinical factors are associated with these complications. Our hypothesis is that significant complications related to urethral stricture are common and that patient demographics are associated with these complications.

METHODS

Institutional ethics board approval was obtained for a retrospective review of patients presenting for evaluation and management of suspected urethral stricture over an 11-year period from January 2005 to December 2016. Initially, 1851 patients with the clinical suspicion of urethral stricture referred to a single urologist for further management were identified. All pertinent institutional data, referring physician and office records were abstracted into a database and screened by 2 separate individuals to identify potential issues regarding data inconsistencies or integrity. Inclusion criteria included patients over 18 years of age with a diagnosis of a clinically significant urethral stricture confirmed with cystoscopy and retrograde urethrography to stage the stricture with regard to length and location. A clinically significant urethral stricture was defined as the inability to pass a flexible cystoscope of 15.8Fr caliber through the area of stenosis. Patient age, absence or presence of LUTS, stricture location, stricture etiology, stricture length, and diagnostic procedures were recorded. Patients presenting with acute trauma such as pelvic fracture urethral injury and acute straddle injuries were excluded from study. These patients do not have symptoms preceding the trauma, often have suprapubic catheter diversion and usually undergo immediate repair prior to the onset of stricture-related symptoms and complications. However, patients describing a remote history of trauma not requiring acute urologic treatment were included. Patients without complete datasets for all clinical variables were also excluded from study.

A stricture-related complication was defined as an adverse event directly related to urethral stricture identified at the time of initial patient presentation prior to urologic intervention. Complications considered significant were acute urinary retention or difficult catheterization requiring emergent urologic intervention, renal failure, urosepsis, or urethral abscess directly related to urethral stricture. Acute urinary retention was defined by the acute presentation of a patient unable to void requiring emergent intervention. Difficult urinary catheterization was defined as the requirement for emergent urologic intervention in order to place a urinary catheter. Urosepsis was defined as a systemic inflammatory response such as fever, tachycardia, tachypnea, respiratory alkalosis related to a culture positive urinary tract infection. Uncomplicated cystitis, epididymitis, or prostatitis were not included in this definition. Abscess was defined the occurrence of a urethral abscess, periurethral abscess, or necrotizing fasciitis (Fournier's gangrene) directly related to urethral stricture. Renal dysfunction was defined as the occurrence of renal insufficiency (Glomerular filtration rate (GFR) <60 ml/min) directly related to bladder outlet obstruction accompanied by either bilateral hydronephrosis or improvement in renal function with drainage of the bladder. Renal imaging was utilized

selectively based on serum creatinine measurement or clinical suspicion of renal dysfunction. Renal failure related to stricture and/or urosepsis either from urethral abscess or urinary tract infection requiring emergent hospitalization were defined as potentially life-threatening complications.

Descriptive statistics were used to summarize the findings while the occurrence of complications was compared in relation to patient age, symptoms, stricture length, location, and etiology using binary logistic regression.

RESULTS

Of 1023 patients met study criteria while a total of 828 patients were excluded due to either an absence of clinically significant stricture on assessment (n = 356), inadequate stricture staging with regard to length or location (n = 130), patient under 18 years of age (n = 16), stricture due to acute trauma (n = 135), or a lack of complete clinical data (n = 191). Cohort demographics are outlined in Table 1. Mean patient age was 48.0 years with a mean stricture length of 5.0 cm (1-18). The majority (95.6%) of patients described lower urinary tract symptoms at the time of presentation with urethral stricture. The most common stricture location was bulbar (65.6%) followed by penile (18.6%), multisegment (10.6%), and posterior (5.4%). Stricture etiology was most commonly idiopathic (46.3%) followed by iatrogenic (15.0%) and lichen sclerosis (14.9%).

Overall stricture-related complications are described in Table 2. In total, 40.6% (415/1023) of patients had at least one

Table 1. Demographics of the cohort

Demographic	N (%)
Number of patients	1023
Age (y)	48.0 ± 17.1
Preceding lower urinary tract symptoms	978/1023 (95.6%)
Stricture length (cm)	5.0 cm ± 4.1 (1-18)
Stricture length >5 cm	297/1023 (29.0%)
Stricture location	
Penile	190/1023 (18.6%)
Bulbar	670 (65.5%)
Pan urethral	108 (10.6%)
Posterior	55 (5.4%)
Stricture etiology	
Idiopathic	474/1023 (46.3%)
Iatrogenic	153 (15.0%)
Trauma	124 (12.1%)
Lichen sclerosis	152 (14.9%)
Hypospadias	71 (6.9%)
Radiation	49 (4.8%)

Table 2. Complications related to urethral stricture

Complication Related to Urethral Stricture	N (%)
Any complication (%)	415/1023 (40.6%)
Acute urinary retention	334 (32.6%)
Difficult urinary catheterization	164 (16.0%)
Renal failure	32 (3.1%)
Urethral abscess/necrotizing infection/urosepsis	51 (5.0%)
Urethral cancer	2 (0.2%)
Life-threatening complication	72 (7.0%)

complication directly related to urethral stricture including acute urinary retention (32.6%), difficult urinary catheterization requiring emergent urologic intervention (16.0%), urethral abscess/necrotizing infection/urosepsis (5.0%), and renal failure (3.1%). Of note, 7.0% of patients experienced complications deemed to be life-threatening with multiple complications in some individuals.

Clinical factors associated with the occurrence of stricture-related complications are found in Table 3. On univariate analysis (Table 3), patient age (in years) ($P = .03$), absence of LUTS ($P < .0001$), stricture location ($P = .02$), and stricture etiology ($P = .02$) were associated with the occurrence of complications. On multivariate analysis using binary logistic regression (Table 3), increasing stricture length (cm) (OR 1.1; 95%CI 1.1-1.2, $P = .01$), lack of reported LUTS (OR 3.8, 95%CI 1.9-7.3, $P < .0001$), posterior stenosis (OR 3.0, 95%CI 1.3-6.8, $P = .01$), and traumatic strictures (OR 1.6, 95% CI 1.1-2.4, $P = .02$) were associated with higher rates of complications related to urethral stricture.

Factors associated with life-threatening stricture complications are found in Table 4. On univariate analysis (Table 4) absence of pre-existing LUTS ($P = .02$), stricture location ($P = .03$), and stricture etiology ($P < .0001$) were associated with life-threatening complications. While on multivariate analysis (Table 4) stricture etiology, particularly trauma (OR 2.2, 95% CI 1.1-4.6, $P = .03$), and hypospadias (OR 2.5, 95% CI 1.1-6.5, $P = .05$) were associated with an increased risk of life-threatening complications. Strictures related to lichen sclerosus had a lower risk of life-threatening complications (OR 0.2, 95% CI 0.1-0.7, $P = .02$).

DISCUSSION

Urethral Stricture-related Complications

It is well established that urethral stricture adversely impacts patient urinary function and quality of life in many diverse ways but is thought to minimally impact overall health status.⁴⁻⁸ However, in the setting of long-standing lower urinary tract obstruction, elevated urinary tract pressures and an increased risk of chronic infection, patients with urethral stricture have the potential for adverse complications impacting overall health status. Most of the complications related to urethral stricture have been thought to be minor, including genitourinary pain, urethral discharge, uncomplicated urinary tract infection, urethral diverticulum, and urethrocutaneous fistula.⁷⁻⁸ However, more severe complications may occur and can cause significant patient morbidity.³ The incidence and factors associated with these more severe complications remain largely undefined. In this study 40.6% of patients in an “industrialized” country presented with a significant complication directly related to urethral stricture defined as either acute urinary retention, difficult catheterization requiring emergent urologic intervention or renal failure, urosepsis, or urethral abscess. These severe complications are thought to be more common in non-industrialized nations. For example, in a population of patients with urethral stricture in South Africa the incidence of perineal sepsis and renal failure occurs in up to

Table 3. Univariate and multivariate analysis of complications associated with urethral stricture (binary logistic regression)

Clinical Variable	Complication N (%)	Univariate P Value	Multivariate	
			Odds Ratio (95% CI)	P Value
Age (continuous) (y)		.03*	1.0 (0.99-1.01)	.22
Age (quartile)				
18-35 years	101/270 (37.4%)			
36-48 years	94/266 (35.3%)			
49-60 years	106/232 (45.7%)			
61-91 years	114/255 (44.7%)			
Preceding LUTS		<.0001*		<.0001*
None	32/45 (71.1%)		3.8 (1.9-7.3)	<.0001*
Yes	383/978 (39.2%)		Referent	-----
Stricture length (continuous) (cm)		.18	1.1 (1.1-1.2)	.01*
Stricture length (quartile)				
1-2.5 cm	102/279 (36.6%)			
2.6-4.0 cm	136/335 (40.6%)			
4.1-6.0 cm	88/211 (41.7%)			
6.1-18 cm	89/198 (44.9%)			
Stricture location		.02*		.04*
Bulbar	257/670 (38.4%)		Referent	-----
Penile	81/190 (42.6%)		1.3 (0.8-2.0)	.29
Multisegment	44/108 (40.7%)		0.8 (0.4-1.7)	.50
Posterior	33/55 (60.0%)		3.0 (1.3-6.8)	.01*
Stricture etiology		.02*		.02*
Idiopathic	174/474 (36.7%)		Referent	-----
Iatrogenic	72/153 (47.1%)		1.2 (0.8-1.7)	.50
Trauma	60/124 (48.4%)		1.6 (1.1-2.4)	.02*
Lichen sclerosus	50/152 (32.9%)		0.6 (0.3-0.9)	.04*
Hypospadias	34/71 (47.9%)		1.2 (0.7-2.3)	.54
Radiation	25/49 (51.0%)		0.8 (0.3-2.0)	.70

Bold values indicate statistical significance of a p -value < 0.05 .

* $P < .05$. LUTS, lower urinary tract symptoms.

Table 4. Univariate and multivariate analysis of life-threatening complications associated with urethral stricture (binary logistic regression)

Clinical Variable	Complication N (%)	Univariate P Value	Multivariate	
			Odds Ratio (95% CI)	P Value
Age (continuous) (y)		.22	1.0 (0.99-1.01)	.21
Age (quartile)				
18-35 years	13/270 (4.8%)			
36-48 years	18/266 (6.8%)			
49-60 years	25/232 (10.8%)			
61-91 years	16/255 (6.3%)			
Preceding LUTS		.02*		.12
None	7/45 (15.6%)		2.0 (0.8-4.9)	.12
Yes	65/978 (6.4%)		Referent	-
Stricture length (continuous) (cm)		.14	0.9 (1.0-1.2)	.14
Stricture length (quartile)				
1-2.5 cm	12/279 (4.3%)			
2.6-4.0 cm	24/335 (7.2%)			
4.1-6.0 cm	20/211 (9.5%)			
6.1-18 cm	16/198 (8.1%)			
Stricture location		.03*		.13
Bulbar	39/670 (5.8%)		Referent	-
Penile	23/190 (12.1%)		1.3 (0.8-2.0)	.06
Multisegment	6/108 (5.6%)		0.8 (0.4-1.7)	.87
Posterior	4/55 (7.3%)		3.0 (1.3-6.8)	.15
Stricture etiology		<.0001*		<.0001*
Idiopathic	24/474 (5.1%)		Referent	-
Iatrogenic	17/153 (11.1%)		1.2 (0.8-1.7)	.32
Trauma	13/124 (10.5%)		1.6 (1.1-2.4)	.03*
Lichen sclerosus	3/152 (2.0%)		0.6 (0.3-0.9)	.02*
Hypospadias	14/71 (19.7%)		1.2 (0.7-2.3)	.05*
Radiation	1/49 (2.0%)		0.8 (0.3-2.0)	.15

Bold values indicate statistical significance of a *p*-value <0.05.

* *P* <.05

39% and 9% of patients, respectively.^{10,11} However, this study suggests that stricture-related complications and impact on overall patient health may be (to some degree) independent of region.

Factors Associated With Complications

Patients at highest risk for complications on multivariate analysis appear to those with longer strictures (*P* = .01), lack of reported LUTS (*P* <.0001), posterior stenosis (*P* = .01), and traumatic strictures (*P* = .02). Longer strictures may be more likely to cause complications by virtue of increased lower urinary tract pressures. A well-known principle of fluid dynamics states that resistance to flow is directly proportional to the length of obstruction. Thus, it appears that longer strictures are more likely to cause complications. Longer strictures are also more likely to fail endoscopic treatments.¹² However, increasing stricture length is also a well-established risk factor for urethroplasty failure.^{13,14} On balance, given the increased propensity for patients with longer strictures to have associated complications it makes sense to treat these patients more definitively with urethroplasty whenever clinically feasible.

Additionally, patients not reporting preceding LUTS had higher rates of complications. It may be possible that these “asymptomatic” patients have insidious obstruction that goes unrecognized until complications arise. These patients for a variety of reasons may fail to recognize the

typical symptoms of stricture until end stage complications occur. It has been documented that patients tend to overlook voiding/obstructive LUTS in particular when compared to storage symptoms given the gradual onset of voiding symptoms.¹⁵ It may also make sense to treat these patients more definitively with urethroplasty or perhaps follow them more closely after endoscopic intervention given their propensity to develop complications in the absence of lower urinary tract symptoms.

Posterior urethral stenoses are also more commonly associated with complications. These stenoses are likely to be related to pelvic fracture, prior surgery such as prostatectomy or radiotherapy and typically have increased density of fibrosis when compared to other strictures.¹⁶ This may in turn lead to higher grade obstruction and predispose to a higher rate of complications. Likewise, this may be the same reason that traumatic strictures are associated with higher rates of complications. Additionally, in the case of posterior stenoses, it has been our clinical observation that stenoses of the membranous urethra are often unpredictable and can rapidly develop into acute urinary retention possibly owing to the sphincteric nature of the posterior urethra.

While longer strictures, asymptomatic strictures, posterior stenoses, and traumatic strictures are associated with higher rates of stricture-related complications, strictures related to lichen sclerosus had lower rates of complications. While not inherently obvious given the insidious

and progressive nature of most lichen sclerosus strictures, it may be possible that patients with these strictures present earlier due to the preceding cutaneous manifestations of lichen sclerosus.^{17,18} If these patients seek medical attention sooner they may have any associated urethral stricture identified early and undergo intervention prior to the onset of stricture-related complications.

Life-threatening Complications

Overall, 7.0% of our patients presenting with urethral stricture have what could be considered life-threatening conditions directly attributable to the urethral stricture. In 5.0% (51) of patients urosepsis occurred typically related to a urethral or periurethral abscess requiring operative urologic intervention. Urethral stricture is a known risk factor for necrotizing infection and Fournier's gangrene.^{9,19} Urinary obstruction due to stricture can lead to extravasation of infected hypertonic into the perineum, scrotum, and Colle's fascia.¹⁹ In this setting of distal stricture and resultant urethrocutaneous fistula, urinary extravasation will persist and progress. Multiple fistulae can form and then coalesce into abscesses and become what is often referred to as a "watering can perineum." As this infected material tracks along fascial planes necrosis of tissue occurs and necrotizing fasciitis develops. In addition to abscess, 3.1% (32) of patient presented with renal dysfunction and bilateral hydronephrosis directly related to chronic urinary retention caused by urethral stricture. Renal failure even as a potentially reversible event carries a significant health risk.²⁰ Lastly, urethral cancer is a rare (0.2%) but potentially devastating complication associated with urethral stricture.²¹ Chronic infection is associated with the development of squamous cell carcinoma. With long-standing inflammatory urethral strictures in the elderly, one should always exercise a high index of suspicion and be aware of the possibility of malignant degeneration.²¹ Certain stricture etiologies appear to be at risk for these life-threatening complications; in particular, traumatic and hypospadias strictures. As mentioned traumatic strictures are more likely to have full thickness spongiofibrosis predisposing to higher grade obstruction and potential for urinary extravasation. Likewise, hypospadias strictures are more likely to have deficient corpus spongiosum and attenuated Dartos fascia which could also predispose to more complicated infections, extravasation, abscess formation, and sepsis. It would appear prudent to treat these types of stricture more aggressively with urethroplasty or at least monitor them more frequently for recurrence after endoscopic treatment.

Limitations

This study does have some inherent limitations. This is a retrospective analysis of patients with urethral stricture referred to a single urologist and this may incur a selection bias. Additionally, complications were identified based on the initial presentation of the patient prior to urologic assessment. This may introduce a recall bias.

Definitions of the exact complications related to urethral stricture may also differ from center-to-center and this could affect the incidence of these complications and potentially limit the generalizability of these results. It is also possible that these patients represent a more severe population of patients with urethral stricture given that a significant portion of these patients were tertiary referrals to a reconstructive urologist for consideration of urethroplasty. However, many patients in this cohort were also referred through a general urologic referral base both emergently (on-call) and electively. In its totality, this population likely represents the typical spectrum of patients with urethral stricture in an industrialized contemporary population.

CONCLUSION

Urethral stricture is frequently a morbid condition. Patients with longer strictures, posterior stenoses, absence of preceding LUTS and traumatic strictures are at highest risk for complications related to urethral stricture. Although urethroplasty has the potential to improve the symptoms of all patients with urethral stricture, patients with these high-risk characteristics should perhaps be strongly encouraged to pursue definitive treatment to mitigate these risks.

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