Endourology and Stones

Symptoms Associated With Long-term Double-J Ureteral Stenting and Influence of Biofilms

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OBJECTIVE	To assess the symptoms associated with long-term Double-J ureteral stenting including the influence of biofilms on ureteral stents.
METHODS	Patients with long-term (>8 weeks) uni- or bilateral ureteral stents completed the Ureteral Stent Symptoms Questionnaire (USSQ) at the day of stent exchange. Repeated assessment of patients was possible to allow for analysis of intraindividual changes. Assessment of biofilm mass on the stents was performed according to a validated method, its correlation with the USSQ total score was defined as primary outcome. Secondary outcomes included further analyses of stent-associated symptoms and their temporal course.
RESULTS	A total of 87 stent indwelling periods in 35 patients were investigated. Median USSQ total score did not differ significantly between unilateral and bilateral stenting (42 vs 39 points; $P = .17$). An increasing total stent treatment time up to study inclusion did not correlate with the USSQ total score, but was significantly correlated with less urinary symptoms and a better quality of life. USSQ total score and subscores within individual patients did not significantly increase or decrease over the sequence of stent indwelling periods. Higher total biofilm masses were not associated with higher USSQ total scores or subscores.
CONCLUSION	Long-term Double-J stenting provides a valuable treatment option, if stent-associated symptoms are low during the initial indwelling period. Thus, symptoms remain stable over the long-term course and the majority of patients are satisfied with the treatment. Furthermore, biofilm formation on ureteral stents does not seem to be the relevant driver of symptoms. UROLOGY 134: 72−78, 2019. © 2019 Elsevier Inc.

Ethical Approval: *All procedures performed involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.*

Informed Consent: *Informed consent was obtained from all individual participants included in the study.*

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Temporary drainage of the upper urinary tract by Double-J ureteral stents (DJs) is a urological standard procedure to assure renal function and to treat pain caused by ureteral obstruction. There are various reasons for long-term ureteral stenting. Thus, definitive surgical treatment is often omitted in patients who are unfit for major surgery or due to patient's preference.

Percutaneous nephrostomies represent an alternative treatment in such patients, but are often associated with lower patient comfort and quality of life (QoL).[1] Moreover, expandable metallic ureteral stents (EMUS) can be used for ureteral stenting. A recent medical technology guidance published by the National Institute for Health and Care Excellence (NICE) showed that EMUS (eg, Memokath) decrease costs in patients expected to require an ureteral stent for at least 30 months.[2] However, the procedure is technically more demanding and feasibility of EMUS is limited in the case of multiple and long strictures, and strictures including the ureteric orifice or pelvic-ureteric junction.[3]

Therefore, DJs are still often used for long-term ureteral stenting. For short-term ureteral stenting, a clear side

effect profile has been shown[4,5] and prevention and treatment of stent-associated symptoms is limited.[6,7] In general, the pathophysiology of stent-associated morbidity is poorly understood. Lower urinary tract symptoms are supposed to be caused by mechanical irritation of the urothelium and nerves, especially in the bladder trigone.[8-10] Furthermore, the impact of biofilms on stent related morbidity has been discussed controversially.[11,12] Since biofilms have been shown to occur more frequently and in increasing amounts with time,[13] the influence on stent related morbidity seems to be of particular interest in this cohort.

Up to now, only very few studies report on symptoms and tolerance of long-term ureteral stenting with DJ stents.[8,13,14] All of them are limited by the use of nonvalidated questionnaires for the investigation of stent-related symptoms and the influence of biofilms on stent related morbidity has not been assessed so far.

Due to this lack of data on morbidity associated with long term DJ ureteral stenting, we performed this prospective observational study.

MATERIALS AND METHODS

Study Setting
The study was approved by the local ethics committee (BASEC 2016-00779) and registered at clinicaltrials.gov (NCT02871609). Patients with uni- or bilateral, long-term (minimum of 8 weeks) indwelling DJs undergoing exchanges on a regular base were prospectively included in the study between July 2016 and November 2018. Reasons for ureteral stenting included benign or malign diseases. Exclusion criteria were ongoing therapy of lower urinary tract symptoms (eg, over active bladder, urinary incontinence, chronic prostatitis, and chronic pelvic pain syndrome), insufficient language skills or cognitive impairment. Patients could be included several times at different time points of stent exchange to allow for an assessment of intraindividual variability.

A Percuflex Plus ureteral stent (Boston Scientific, Natick, MA) with a diameter of 6 French and a length of 26 or 30 cm according to patient's height and surgeon's estimation was used in all patients. Patients were interviewed preoperatively about clinical signs of urinary tract infection (UTI) (eg, pronounced dysuria, fever). In the case of suspected clinically relevant UTI, the operation was postponed which was not the case in any of the included patients.

Patients completed the German version of the Ureteral Stent Symptoms Questionnaire (USSQ)[15] prior to stent exchange to rate the previous indwelling period. Urine samples (sediment and urine culture) were collected before stent exchange. A single-shot Co-trimoxazole (800/160 mg per os) was routinely given 1 hour before stent exchange according to recent recommendations[16] if not contraindicated (eg, by allergies or results of previous urine cultures).

Correlation between total biofilm mass on the stent surface and USSQ total score at the time of stent removal was defined as the primary outcome. Secondary outcomes included the association of USSQ subscores with the biofilm mass and a general assessment of stent-associated symptoms and their clinical course using the USSQ and its subscores.

Biofilm—Extraction and Analysis
Stents were exchanged using Seldinger technique, cut in half and stored in collection tubes at −16°C. Bilateral stents were collected in separate tubes. Biofilm examinations were performed by the Laboratory for Biointerfaces (Empa, Swiss Federal Laboratories for Materials Science and Technology, St. Gallen, Switzerland) according to a protocol described in detail elsewhere.[17] Stent halves were passed through a tapered pinhole in a stainless steel plate. Extracted biofilms (consisting of crystalline encrustations, extracellular matrix, and bacterial biofilms) were suspended in 2 mL saline solution, collected and balanced in 2 mL microcentrifuge tubes. After centrifugation for 5 minutes at $14,100 \times g$, the supernatant was removed and the pellet wet weight was determined using an analytical balance. Biofilms were examined without a subdivision of their components. For patients with bilateral stenting, data were analyzed in 2 ways: the sum of both sides ("total biomass") or the mean ("mean biomass per stent").

Statistical Analysis
The 2 biomass measurements and the USSQ scores were compared between 1- and 2-sided stenting with mixed-effects models including patient identity as random effect. Biofilm mass had a positively skewed distribution. For analyses that assume a normal distribution, data were log-transformed, and plotted with a logarithmic axis. Associations between USSQ, biofilm mass and the duration of stenting were analyzed separately among and within patients. Associations among patients were described by scatter plots and Spearman rank correlations with 95% CI using only data from 1 (eg, the first) stent indwelling period. Associations within patients (for patients studied after several stent indwelling periods) were described by line plots and by reporting regression slopes with 95% CI from mixed-effects models with random intercepts for the patients.

RESULTS

Patients and Perioperative Findings
Four patients had to be excluded from the analysis (wrong type of ureteral stent, questionnaires answered inappropriately). Thus, totally 87 stent indwelling periods could be investigated. The study included 35 patients: 18 with a single and 17 with 2-8 successive stent indwelling periods. Table 1 shows the demographics and clinical characteristics of the patients included.

Considering all stent exchanges ($n = 87$), Bacteriuria was found in 24% prior to the operation. The most common bacteria were: *Enterococcus faecalis* (33%), *Escherichaia coli* (24%), *Klebsiella pneumoniae* (14%), and Staphylococcus *epidermidis* (14%). Bacteria were found most frequently to be resistant toward Ciprofloxacin (42.9%), followed by Co-Amoxicillin (23.8%), Co-trimoxazole (14.3%), and Cefuroxime (9.5%). The risk of bacteriuria was unrelated to stent indwelling time (median 12 weeks for both groups, Wilcoxon test, $P = .79$). During the 87 stent indwelling periods, patients were prescribed antibiotics nine times ($5\times$ Ciprofloxacin, $4\times$ Co-Trimoxazole). Diagnosis and treatment were performed in an outpatient setting by the patients' general practitioner and urine cultures were not available. One patient took an alpha-blocker and three patients took antimuscarinics during a stent indwelling period.

Median duration of surgery was 17 minutes (range 3-137).

Stent Associated Symptoms
Figure 1 shows the distributions of the USSQ total scores and selected subscores/single items. While the USSQ total score was below 60 in the majority of patients, some very high total scores

Table 1. Clinical characteristics of study participants (n = 35). (Patient characteristics relate to the time of study inclusion. PCN, percutaneous nephrostomy)

Patient Characteristics	Median [range]	Stent Indication	n (%)	Stent Indwelling Periods in Study	n (%)
Age (y)	75 [33-93]	Benign	14 (40%)	1	18 (51.4%)
BMI (kg/m^2)	24.6 [17.7-38.8]	Ureteral stricture	7 (50%)	2	5 (14.3%)
Duration of Double-J treatment at the time of study inclusion (mo)	12 [2-84]	Ureteropelvic junction obstruction	5 (35.8%)	3	3 (8.6%)
Stent change interval (wk)	12 [8-25]	M. Ormond	1 (7.1%)	4	3 (8.6%)
	n (%)	Pelvic inflammatory disease with ureter compression	1 (7.1%)	5	2 (5.7%)
Male/female	26 (74.3%)/9 (25.7%)	Malign	21 (60%)	6	1 (2.9%)
Diabetes mellitus	6 (17.1%)	Prostate cancer	13 (61.9%)	7	2 (5.7%)
Chronic renal insufficiency	15 (42.9%)	Rectal cancer	3 (14.2%)	8	1 (2.9%)
Unilateral/bilateral stent	25 (71.4%)/10 (28.6%)	Ovarian cancer	2 (9.5%)	Reasons for study withdrawals:	n (%)
ASA Score:	n (%)	Urothelial cancer	1 (4.8%)	Total	21 (60%)
I	4 (11.4%)	Endometrial cancer	1 (4.8%)	Death	7 (33.3%)
II	18 (51.4%)	Liposarcoma	1 (4.8%)	Definitive treatment	6 (28.6%)
III	12 (34.4%)			Change stent to EMUS	4 (19%)
IV	1 (2.9%)			Change stent to PCN	2 (9.5%)
				Change to other type of ureteral stent	2 (9.5%)
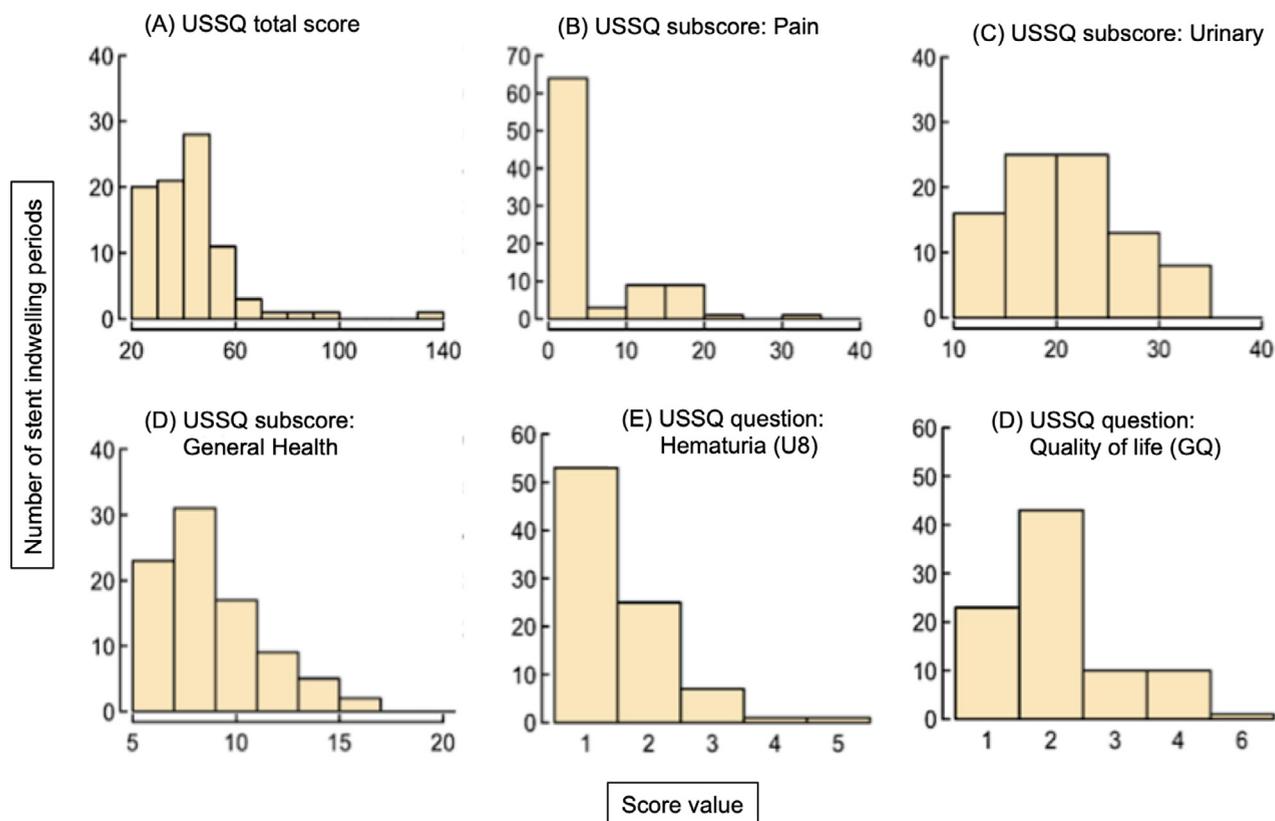
Figure 1. Distributions of the USSQ total score and selected subscores and single items. (Higher USSQ scores, subscores, and values for single items indicate more symptoms. Numbers of stent indwelling periods (y-axis, totally n = 87) are grouped by extend of symptoms (x-axis).) (Color version available online.)
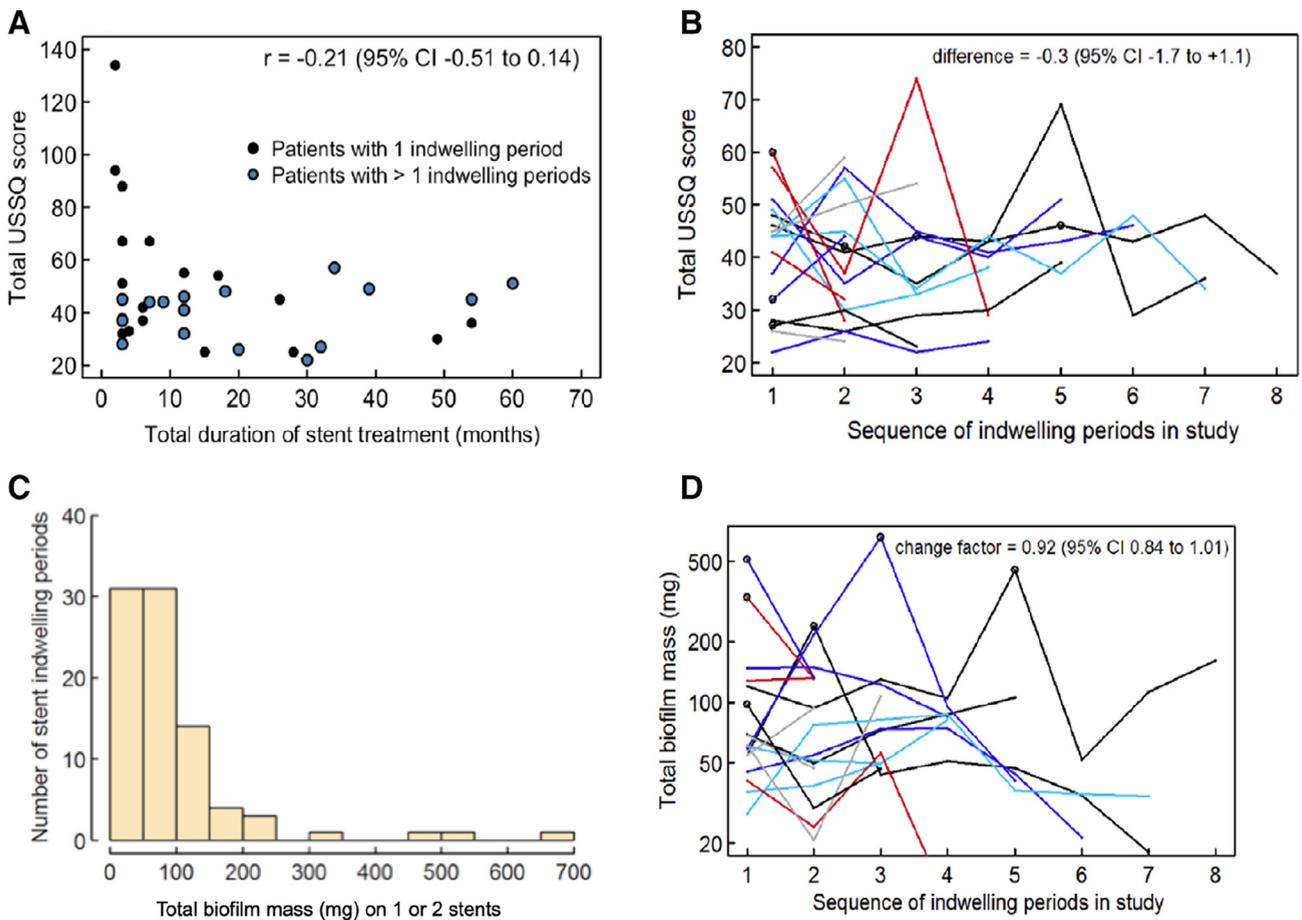
Figure 2. Correlation of USSQ total score and the total duration of stent treatment up to study inclusion across the 35 patients (A) and change in USSQ total score through time within patients with two or more stent exchanges within the study (B). Scores are plotted against each patient's sequence of stent indwelling periods in (B). USSQ scores, which corresponding biofilm mass values are much higher than others (see panel D), are indicated by circles in panel B. Distribution of total biofilm mass considering all indwelling periods (C). Associations between total biofilm mass and sequence of indwelling periods within the different patients (D). Biofilm mass values that are much higher (more than twice as much) than others for a given patient are indicated by circles. The corresponding USSQ scores are also circled in (B). (Color version available online.)

were reported by patients with a single stent indwelling period (Fig. 2A), the same was found for individual subscores.

Median USSQ total score did not differ significantly between unilateral and bilateral stenting (42 points [23-134] vs 39 points [22-54]; $P = .17$).

Median subscores were 21 (12-35) for urinary symptoms, 0 (0-33) for pain and 8 (5-17) for general health. Pain attributed to the ureteral stent was reported in only 23 (26%) of the stent indwelling periods, 48% of the patients with pain required analgesics to control the pain or discomfort associated with the stent.

According to the USSQ general question (GQ), patients were predominantly (86%) "*at least mostly satisfied*" with ureteral stenting, while being "*mostly dissatisfied*" (13%) or "*unhappy*" (1%) was reported less frequently.

Grade 1 adverse events (AEs) according to CTCAE[18] at least possibly related to ureteral stenting occurred during 34 (39%) of the stent indwelling periods. Grade 2-4 AEs were found in 16 (18%), 3 (3%), and 1 patient (1%; life threatening urosepsis), respectively.

The duration of stenting up to study inclusion did not correlate significantly with the USSQ total score among the 35 patients ($r = -0.21$, $P = .23$; Fig. 2A), but was significantly correlated with less urinary symptoms and a better stent related QoL (GQ) (Tab. 2). USSQ total score and subscores within individual patients did not significantly increase or decrease over the sequence of stent indwelling periods ($P = .64$, Fig. 2B), indicating stable symptoms in these patients.

Biofilm Examination and Correlation With Stent Related Symptoms

Biofilm mass had a strongly skewed distribution (Fig. 2C), similar results were seen when considering data from first stent indwelling period or all periods. Total biofilm mass was significantly larger ($P = .03$) with 2-sided stenting (median 84 mg [21-658]) compared to one-sided stenting (median 55 mg [10-450]). Two stents inserted simultaneously (same patient) had a similar biomass: median difference 12.9 mg [0.9-119.5]. Mean biofilm mass per stent did not differ significantly with 1- or 2-sided stenting ($P = .59$).

Associations within patients showed that the mean change factor of the total biofilm mass from one indwelling period to the next (Fig. 2D) and mean biofilm mass per stent were not significantly different from 1 ($P = .06$ and .07, respectively). Although

Table 2. Correlations between USSQ total score and selected subsscores or single items and duration of stent treatment and extracted biofilm mass

	Total Treatment Duration up to Study Inclusion	P Value	Total Biofilm Mass	P Value	Mean Biofilm Mass	P Value
USSQ total score	−0.21 (−0.51 to 0.14)	.23	−0.52 (−0.74 to −0.20)	.001	−0.51 (−0.73 to -0.19)	.002
USSQ subscore: Urinary	−0.38 (−0.64 to −0.05)	.02	−0.42 (−0.67 to −0.08)	.01	−0.37 (−0.64 to −0.03)	.03
USSQ subscore: Pain	−0.13 (−0.45 to 0.21)	.45	−0.42 (−0.67 to −0.09)	.01	−0.36 (−0.63 to −0.02)	.03
USSQ subscore: General Health	−0.12 (−0.43 to 0.23)	.51	−0.25 (−0.54 to 0.09)	.15	−0.23 (−0.53 to 0.11)	.18
USSQ Question: Hematuria (U8)	−0.14 (−0.45 to 0.21)	.43	0.11 (−0.23 to 0.43)	.53	0.13 (−0.21 to 0.44)	.46
USSQ Question: Quality of life (GQ)	−0.62 (−0.80 to −0.33)	<.001	−0.47 (−0.70 to −0.14)	.005	−0.32 (−0.60 to 0.02)	.06

Correlations are calculated across the 35 patients in the first indwelling period and are given with 95% confidence intervals. For patients with bilateral stenting, data were analyzed in 2 ways: the sum of both sides ("total biomass") or the mean ("mean biomass per stent").

a few biofilm mass values were much higher than others of the same patient, the corresponding USSQ scores (Fig. 2B) were not particularly high, meaning that there was no association between unusually high biofilm mass and more severe symptoms.

The USSQ total score correlated negatively with total and mean biofilm mass after the first indwelling period (Table 2). This was mainly due to 3 patients with exceptionally high USSQ total score and low biofilm mass, studied at a single indwelling period followed by definitive surgical treatment. Significant negative correlations were also found for the USSQ subscores urinary symptoms and pain and for QoL related to ureteral stenting (GQ). However, none of the correlations were significant after the second and third indwelling periods and mean changes in USSQ scores associated with successive stent indwelling periods within patients were all not significant.

DISCUSSION

This prospective study provides novel insights on symptoms associated with long-term DJ ureteral stenting including the influence of biofilms. We could show that permanent DJ stenting provides a valuable treatment approach in selected patients. If stent associated symptoms are low during the first indwelling periods, symptoms remain stable over the course and the majority of patients are satisfied with the treatment. Nevertheless, stent-related symptoms and AEs still represent a relevant problem for some patients, but biofilm formation on ureteral stents does not seem to be the relevant driver of these symptoms. Moreover, we could show that symptoms remain constant over time, which allows for improved patient selection and determination of indwelling intervals.

Previously, Lim et al[14] investigated 20 patients who underwent stent treatment up to 38 months with stent replacement every 3 months using the International Prostate Symptom Score and a linear visual analogue scale for pain. Storage symptoms and pain both improved over time. Moreover, studies on short-term ureteral stenting (eg, average stent indwelling time of 18 or 28 days, respectively[8,12]) reported on a reduction of USSQ Urinary and Pain subscore or visual analogue scale with increasing indwelling time.

In contrast, an improvement was only found for urinary symptoms in our study, while the USSQ total score and pain subscore did not significantly decrease. These differences might mainly be caused by the median duration of Double-J treatment at the time of study inclusion of 12 months (2-84) in our study. However, none of the symptoms showed deterioration over the stent indwelling time.

Despite the presence of more stent-material that might cause mechanical irritation, there was no significant difference in symptoms between uni- or bilateral stenting.

Compared to a recent study on short-term stenting before ureterorenoscopy also using the USSQ and the same type of stent,[12] patients with a long-term stent seem to have fewer symptoms. Thus, a lower median USSQ total score (42/39 points (unilateral/bilateral) vs 83 points), a lower proportion of patients suffering from pain (26% vs 83%), and a higher proportion of patients at least "mostly satisfied" (GQ) with ureteral stenting (86% vs 26%) were found in the present study. Consistent with these results, few patients took painkillers or other medications (alpha-blocker, antimuscarinics) to reduce the discomfort associated with the stent.

These findings underline that factors such as underlying disease, anatomical, and inflammatory changes have an influence on the degree of stent-associated symptoms. Moreover, less symptoms have been reported to occur in older patients elsewhere.[19] On the other hand, patients undergoing long-term ureteral stenting that are suffering from severe symptoms are likely to switch to an alternative treatment concept such as percutaneous nephrostomies or definitive surgery, which might bias indirect comparisons (Table 1).

Positive urine cultures were found in 24% and presence of bacteriuria was not associated with stent indwelling time. Remarkably, this rate seems to be very stable, that is, between 21% and 35%,[19,20] and largely independent from the stent indwelling time. Moreover, the most common pathogens were found to be the same (*Escherichia coli* and *Enterococcus*) as with short-term ureteral stenting.[12,20] Complaints of patients with a positive urine

cultures were not analyzed separately, however, recent data could not show a significant relationship between the presence or absence of bacteriuria and stent related symptoms.[12]

Nine patients underwent antibiotic therapy during a stent indwelling period because of a suspected UTI. The lack of urine cultures of these patients before antibiotic treatment represents another limitation of the study. Thus, it remains unclear if patients were treated for UTI or stent associated symptoms similar to UTI. Nevertheless, the use of antibiotics has been shown to have no significant influence on biofilm formation on ureteral stents elsewhere.[21]

Using a validated assessment method,[17] biofilms could be extracted from each of the stents. The total biofilm mass per stent was 36% higher compared to a cohort of stone formers with a median indwelling time of 28 days (19-41)[12] assessed with the same method.

The USSQ total score, USSQ urinary symptoms, pain, and QoL subscores were correlated negatively with the biofilm mass after the first indwelling period. This negative correlation was mainly due to 3 patients with exceptionally high USSQ total score and low biofilm mass, studied at a single indwelling period and might also be caused by an earlier stent exchange in patients with more severe symptoms. As a consequence, a lower biofilm mass might be found on these stents. In addition, no significant correlations of biofilms and symptoms were found for the second and third stent exchange. Therefore, our data strongly suggests that biofilms on long-term ureteral stents are not a relevant driver of stent-associated symptoms, as previously described for short-term ureteral stenting.[12]

Since a validated and specific questionnaire was never used before in terms of long-term ureteral stent application, this is a clear strength of the study. To our knowledge, this is also the first study investigating the influence of biofilms on stent-associated symptoms in patients undergoing long-term stenting. The use of an improved and validated biofilm extraction method allowed for a standardized assessment of the biofilm and a comparison to previous studies as well. Moreover, the same stent type was used in all of the patients.

Although patient inclusion in the study was prospective, some of the patients already had long-term indwelling stents at the time of inclusion. As patients with very strong symptoms are likely to undergo alternative treatment approaches, the study is prone to selection and attrition bias. As another limitation, cultivation or cultivation-independent examinations of biofilms other than biofilm mass was not performed.

CONCLUSION

Using validated patient-reported outcome measures, we could show that permanent DJ stenting provides a valuable treatment concept in selected patients and biofilm formation on long-term ureteral stents does not aggravate the stent related symptoms. Moreover, symptoms remain constant over time, which allows for improved patient selection and determination of indwelling periods. Despite a good acceptance of long-term stenting in many patients, further approaches have to be pursued to reduce stent-associated morbidity, which is still considerable in some patients.

References

1. Aravantinos E, Anagnostou T, Karatzas AD, Papakonstantinou W, Samarinas M, Melekos MD. Percutaneous nephrostomy in patients with tumors of advanced stage: treatment dilemmas and impact on clinical course and quality of life. *J Endourol Endourol Soc.* 2007;21:1297–1302. https://doi.org/10.1089/end.2006.0104.
2. Eaton Turner E, Jenks M, McCool R, et al. The Memokath-051 stent for the treatment of ureteric obstruction: A NICE medical technology guidance. *Appl Health Econ Health Policy.* 2018;16:445–464. https://doi.org/10.1007/s40258-018-0389-3.
3. Fiuk J, Bao Y, Calleary JG, Schwartz BF, Denstedt JD. The use of internal stents in chronic ureteral obstruction. *J Urol.* 2015;193:1092–1100. https://doi.org/10.1016/j.juro.2014.10.123.
4. Betschart P, Zumstein V, Piller A, Schmid HP, Abt D. Prevention and treatment of symptoms associated with indwelling ureteral stents: a systematic review. *Int J Urol.* 2017. https://doi.org/10.1111/iju.13311.
5. Joshi HB, Stainthorpe A, Keeley Jr. FX, MacDonagh R, Timoney AG. Indwelling ureteral stents: evaluation of quality of life to aid outcome analysis. *J Endourol Endourol Soc.* 2001;15:151–154. https://doi.org/10.1089/089277901750134421.
6. Walker NA, Bultitude MF, Brislane K, Thomas K, Glass JM. Management of stent symptoms: what a pain!. *BJU Int.* 2014;114:797–798. https://doi.org/10.1111/bju.12534.
7. Abt D, Warzinek E, Schmid HP, Haile SR, Engeler DS. Influence of patient education on morbidity caused by ureteral stents. *Int J Urol.* 2015;22:679–683. https://doi.org/10.1111/iju.12782.
8. Irani J, Siquier J, Pires C, Lefebvre O, Dore B, Aubert J. Symptom characteristics and the development of tolerance with time in patients with indwelling double-pigtail ureteric stents. *BJU Int.* 1999;84:276–279.
9. Pidsudko Z. Distribution and chemical coding of neurons in intramural ganglia of the porcine urinary bladder trigone. *Folia Histochem Cytobiol.* 2004;42:3–11.
10. Zumstein V, Betschart P, Albrich WC, et al. Biofilm formation on ureteral stents - Incidence, clinical impact, and prevention. *Swiss Med Wkly.* 2017;147:w14408. https://doi.org/10.4414/smw.2017.14408.
11. Bonkat G, Rieken M, Muller G, et al. Microbial colonization and ureteral stent-associated storage lower urinary tract symptoms: the forgotten piece of the puzzle? *World J Urol.* 2013;31:541–546. https://doi.org/10.1007/s00345-012-0849-6.
12. Betschart P, Zumstein V, Buhmann MT, et al. Influence of biofilms on morbidity associated with short-term indwelling ureteral stents: a prospective observational study. *World J Urol.* 2018. https://doi.org/10.1007/s00345-018-2569-z.
13. Kawahara T, Ito H, Terao H, Yoshida M, Matsuzaki J. Ureteral stent encrustation, incrustation, and coloring: morbidity related to indwelling times. *J Endourol Endourol Soc.* 2012;26:178–182. https://doi.org/10.1089/end.2011.0385.
14. Lim JS, Sul CK, Song KH, et al. Changes in urinary symptoms and tolerance due to long-term ureteral double-J stenting. *Int Neurourol J.* 2010;14:93–99. https://doi.org/10.5213/inj.2010.14.2.93.
15. Abt D, Dotzer K, Honek P, et al. The German linguistic validation of the Ureteral Stent Symptoms Questionnaire (USSQ). *World J Urol.* 2016. https://doi.org/10.1007/s00345-016-1875-6.
16. EAU Guidelines on Urological Infections. http://uroweb.org/guideline/urological-infections/. Accessed June 2016.
17. Buhmann MT, Abt D, Altenried S, et al. Extraction of biofilms from ureteral stents for quantification and cultivation-dependent and

-independent analyses. *Front Microbiol.* 2018;9:1470. https://doi.org/10.3389/fmicb.2018.01470.

18. National Cancer Institute Common Terminology Criteria for Adverse Events v4.03 (CTCAE). http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf.

19. Leibovici D, Cooper A, Lindner A, et al. Ureteral stents: morbidity and impact on quality of life. *Isr Med Assoc J.* 2005;7:491–494.

20. Weber A, Zumstein V, Betschart P, et al. Prediction of bacteriuria based on clinical or laboratory parameters in patients with indwelling ureteral stents before ureterorenoscopy should not substitute for urine cultures. *J Endourol Endourol Soc.* 2018;32:739–745. https://doi.org/10.1089/end.2018.0256.

21. Riedl CR, Plas E, Hubner WA, Zimmerl H, Ulrich W, Pfluger H. Bacterial colonization of ureteral stents. *Eur Urol.* 1999;36:53–59. doi:19927.