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# Complications of upper urinary tract stenting

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**Abstract:** *Restoration of the passage of urine along the upper urinary tract is routinely provided by the installation of external or internal drainage. Due to its objective advantages, internal drainage has been successfully used in upper urinary tract surgery. The review outlines the problems associated with the use of internal stents, namely: difficulties in installation, migration, reflux and obstruction of the stent, bacterial colonization of the stent, the development of functional and morphological changes in the drained segment of the urinary tract.*

**Key words:** *biofilm, reflux, migration, obstruction, stent.*

**Introduction:** The restoration of the passage of urine along the upper urinary tract is routinely provided by the installation of external or internal drainage [1-7]. Such unconditional advantages of the latter method, as ease of installation, the non-necessity of X-ray or ultrasound control, the absence of external drainage and the risk of nosocomial drainage infection, make it very popular among practicing urologists [2, 8-11]. In this regard, internal drainage is successfully used and recommended by many authors after endourological manipulations on the upper urinary tract, during reconstructive plastic surgery on the ureter and pelvic ureter segment, radical surgery of muscle-invasive bladder cancer [1, 2, 12-21]. The problems of drainage complications are less covered in the literature. The disadvantages of internal drainage include difficulties or impossibility of endoscopic installation and removal of stents in obstructive pathology of the vesicourethral segment, migration of the stent and its inadequate positioning during installation without X-ray control, obstruction of the stent by inflammatory detritus, salts, blood clots, limited timing of internal drainage, vesicoureteral reflux (PMR) with the development of refluxnephropathy and ascending infection [22-32]. There are isolated publications about violations of motility and microcirculation detected in the experiment in the stented ureter, sclerotic changes in its wall even against the background of short drainage [24, 26, 33, 34]. In this review, we attempt to consider the main difficulties associated with stenting, and in this regard, substantiate possible ways to overcome them.

Technique of stenting and stent removal. To ensure adequate positioning of the stent, reducing the frequency of urinary tract perforations, combined endoscopic, X-ray and ultrasound monitoring is necessary [35-37], at the same time, there are publications on the rather high efficiency (up to 71%) of retrograde ureter stenting under cystoscopic control [38]. At the same time, it is reported that the success rate in implantation of polyurethane stents is somewhat (statistically not significantly) higher compared to metal ones – 97.4 and 82.7%, respectively [19, 30].

The question of the need to remove a metal stent becomes relevant when it is obstructed. The duration of operation of plastic stents is shorter compared to metal ones, but their replacement is technically easier. There is no consensus on the effectiveness of the use of coated and uncoated metal stents. A fairly large number of studies, mainly single-center, demonstrate the advantages of polymer-coated metal stents [17, 19, 34, 39]. However, there are reports based on a meta-analysis of 8 randomized and 9 prospective studies with a sample of 1,743 patients in which there were no differences in the rate of obstruction depending on the metal stent used [40, 41]. Coated metal stents, like plastic ones, can be removed endoscopically in most cases. Removal of uncoated metal stents is not always feasible, therefore there is a need for recanalization of their lumen, which can account for up to 14.3–32.0% of all implantations. For these purposes, holmium laser ablation and intraluminal stenting are used, or only the latter, and the use of plastic stents is even preferable in this case [42, 43].

Retrograde ureteral stenting and stent removal are associated with technical difficulties in the pathology of the vesicourethral segment. The exclusion of cystoscopy for removal of the ureteral stent is also relevant for pediatric urology. A. Kajbafzadeh et al. presented the results of 523 pyeloplastics performed on children by laparoscopic access with the installation of a Double J stent, the proximal end of which was fixed to a 3 Ch tube removed through a pyelotomy incision on the skin. Transdermal stent removal was performed 3-4 weeks after surgery on an outpatient basis. The advantages of this approach include the absence of the need for postoperative catheterization and cystoscopy for stent removal, as well as a reduction in the length of stay and frequency of postoperative complications – in 8.4% of cases, minor hematuria and pyelonephritis attack were noted, there were no urinary congestion and recurrence of stricture during 6 months of follow-up [11]. The further evolution of transdermal stents consisted in the creation of a segmental stent in limited contact with the ureteral surface (transanastomotic stent). For this purpose, a Double J-stent 5-7 cm long was used, the curl of which was located in the pelvis, and the stent was removed according to the method described above by a tube removed through the wall of the pelvis or the kidney parenchyma onto the skin.

The publications for 2014 described 172 observations of the use of these stents in children with an average age of 5.6 years. The authors note a total reduction in complications compared to using a Double J-stent from 35% to 7,4–13,0% [20, 44, 45].

Migration of the stent. The frequency of migration of stents is determined by their design and the specific clinical situation, such as the correspondence of the diameter of the stent and dilatation of the drained hollow organ, the duration of drainage, etc. [19, 30, 39]. In relation to the stenotic lesion of the ureter, proximal and distal migration are distinguished. With regard to urinary stents, the migration problem is relevant for segmental drainage, i.e. for metal stents, especially with a polymer coating. The frequency of migration of uncovered stents, according to the literature, ranges from 14.5 to 23.0%, this indicator for the first covered stents reached 81% [35, 43]. The development of new fixing devices has reduced the frequency of migration of the UVENTA™ coated stent (Taewoong Medical, Korea) and new hybrid analogues to 5,9–6,6% [34, 39]. The risk factors include the degree of dilation of the upper urinary tract, the diameter of the stent used, the presence of a polymer coating and the duration of stenting. The frequency of migration of Double J stents is small and is only 1.9-3.7%, which is associated with total splinting of the ureter, fixation of curls in the pelvis and bladder. This complication develops when the lengths of the stent and ureter do not match and is somewhat more common when using thermolabile silicone stents [19, 30, 46].

Stent obstruction. Encrusting ureteral stents with urinary salts shortens their service life and increases the risk of obstructive complications, the frequency of which reaches 50-74%. In vitro studies have shown that the presence of uropathogens increases the adhesion of salts, in particular phosphates, magnesium and ammonium, to the stent surface [43, 47, 48]. In vitro models have proved that the presence of a protein matrix in urine increases lithogenesis on the stent surface by 7-

12 times. Spectrometric and chromatographic analyses of salt deposits of ureteral stents have shown that there is selectivity in the formation of a protein matrix and α1-antitrypsin, γ-globulins and nuclear proteins have the greatest affinity [49]. Vesicoureteral reflux, although it prevents the adhesion of salts, does not exclude the latter. Thus, endoluminal optical coherence tomography of 14 removed stents (the average stenting period is 100 days) revealed a more pronounced narrowing of the lumen to 10-35% of the initial one in the proximal parts of the stent compared with the distal ones [28]. A more extensive study of 300 removed stents established a correlation between the frequency of obstruction and the duration of drainage. Obstruction of the lumen was detected in 155 (47%) stents, and its frequency was 26.8% when the stent was in the ureter for less than 6 weeks, 56.9% for 6-12 weeks and 75.9% for more than 12 weeks. In general, difficulties with cystoscopic removal of stents occurred in 46 (13.9%) cases, and 3 of them could not be removed cystoscopically. The average period of stay of stents before the development of intraluminal obstruction was 72 days and 31 days before the formation of concretion at the renal end for non-removable stents [31, 47].

Often, due to lithogenesis with the formation of concretions at the renal and vesicular ends of the Double J stent, multi-stage percutaneous and transvesical lithotripsies are performed to remove it [50]. Thus, V. Pais et al. 36 observations of encrusted stents are reported, the average stay of which was 28.2 months. At the same time, in half of the cases, patients were not informed about the established stent, and in 3 cases such salt encrustation occurred in less than 3 months. Combined percutaneous nephrolithotripsy and cystolithotripsy made it possible to remove residual stents [30, 51].

Obstruction of the ureteral Double J stent is not always associated with lithogenesis. Having a sufficiently large length and a relatively small internal lumen, Double J-stent is characterized by a high risk of obstruction by inflammatory detritus or blood clots. Thus, there are complaints in the literature about Double J stents used for drainage in acute obstructive pyelonephritis, when the frequency of inadequate functioning of the stent with the progression of the inflammatory process in the kidney reached 27.5–44.0%. Difficulties in ensuring hemostaticity of laparoscopic or robotic suture of ureteropyeloanastomosis during plasty of strictures of the pelvic-ureteral segment were accompanied by Double J-stent obstruction and prolonged urine leakage in 13-25.7% of patients, which required stent replacement or percutaneous nephrostomy in 22-41% of patients with similar complications [20, 21, 52].

Obstruction of metal urinary stents in most cases is associated with hyperplastic mucosal growths and the formation of inflammatory strictures at the ends of the stent, as well as with neoplastic occlusion of the lumen and salt encrustation. The average period of development of such complications is 8-16 months [7, 34, 53]. The use of polymer-coated metal stents makes it possible to reduce the frequency of tumor invasion and obstruction by granulation tissue from 70.0 to 17.6%, but the use of polymer coatings increases the likelihood of adhesion to the stent surface of both bacteria and urinary salts with the formation of biofilms [19, 34, 39]. Another solution to this problem may be the use of drug–coated stents - Drug-eluting stents, when antiproliferative agents are used as active substances [7, 43, 54, 55].

Colonization of the stent by bacteria, formation of biofilms, antibiotic resistance. Experimental studies in vitro and in vivo have shown the presence of genetically determined adhesion factors in a number of microorganisms: E. coli, Pr. mirabilis, Ps. aeruginosa, E. faecium. These include urease-, succinate dehydrogenase- and carbonic anhydrase-positivity, specific surface proteins of the cell wall, the ability to form fimbriae and outgrowths and the genes that determine this [29, 32, 56, 57].

Colonization of internal polyurethane Double J stents develops quite quickly (within hours or days) after installation, the probability of mixed and mycotic infection increases in direct proportion to the timing of stenting and does not correlate with the positivity of uroculture, which is confirmed by both clinical and experimental studies [29, 32, 58]. Thus, during stenting of 60 patients with initially negative bacteriological urine tests, R. Kliś et al. (2014) for periods up to 30, 30-90 and more than 90 days, microflora growth was obtained only in 13.3% of observations, and PCR examination of explanted stents revealed their total infection. The frequency of mixed infections and the degree of obstruction of stents by struvite stones increased with increasing duration of drainage [59].

Interesting data were obtained by studying the surface transmembrane charge of six strains of E. faecalis, which had statistically significant differences depending on the strain. It was found that the strain with the maximum charge had a greater ability to form mixed biofilms with Citrobacter freundii BS5126, Stenotrophomonas malthophilia BS937 and Candida lusitaniae BS8256 [57].

As already mentioned, in most cases, a mixed infection is released from the stent, bacteria of the intestinal group of the Bacteriacae family predominate. The authors, who study in depth the microbiological landscape of stent biofilms, report the frequent detection of anaerobes, representatives of the genera Bacteroides, Clostridium, Fusobacterium, Finegoldia, Prevotella and Veillonella in associations with aerobic bacteria. During bacteriological studies of removed stents and experimental in vitro models, the ability of strains belonging to the species Bacteroides oralis, Clostridium difficile, Clostridium baratii, Clostridium fallax, Clostridium bifermentans, Finegoldia magna and Fusobacterium necrophorum to participate in the formation of mixed biofilms was shown. By itself, the infection of stents of this localization, proven after planned removal, is often not accompanied by a clinic of infectious and inflammatory complications [26, 60]. The biocenosis in the biofilm contributes to the sedimentation of urinary salts on the protein matrix, i.e. lithogenesis, which acts as one of the factors protecting bacteria in the biofilm. In turn, the growth of biofilm causes obstruction of the stent lumen and the development of inflammatory complications. Accordingly, the frequency of local and systemic inflammatory complications increases with increasing drainage time. These complications develop against the background of stent obstruction and require drainage manipulations.

The effect of antibacterial therapy on colonized stents is indistinguishable from zero, which dictates the development of preventive measures for this type of complications [26, 61].

Reflux. After the installation of an internal ureteral Double J-stent, PMR is a standard complication, since the closing function of the vesicoureteral sphincter and cystoid contractions of the ureter itself are disrupted, and in general, signs of PMR detected by ultrasound can characterize adequate patency of the jj-stent [33]. This complication is regarded ambiguously in the literature: some authors consider PMR as a positive factor for reducing lithogenesis on the stent and during drainage against the background of acute obstructive pyelonephritis, since irrigation of the abdominal system occurs on the side of the lesion with bladder urine, which contains excreted antibacterial drugs [10, 28], others, and most of them, indicate negative the sides of this complication [24, 62-65]. The latter consist in hydrodynamic trauma of the stented kidney with the development of pyelotubular reflux, tubular hypertension and sclerotic changes in the kidney; in addition, an ascending path of infection is realized, leading to focal purulent-destructive lesions of the parenchyma and systemic inflammatory complications. These provisions have been proven both in experimental and clinical studies. The frequency of reflux pyelonephritis is determined by the timing of drainage and, according to the literature, ranges from 5.4 to 37.1% [62, 64]. In experiments on explanted pig organocomplexes, it was shown that the pressure value leading to PMR at a stent diameter of 7 Ch is approximately 9 times lower than the same indicator for a stent of 5 Ch, and is 6.2 ± 0.3 cm of water. There are data obtained on in vitro models indicating that reflux during miction, it is leveled due to the capillary effect and discharge through the lateral openings of the

Double J-stent [34, 66]. The weak side of such an in vitro model is the absence of a bladder filling phase, which is accompanied by PMR in a number of patients with ultrasound and clinically.

An attempt to solve the problem of PMR was the creation of antireflux stents with a nipple valve made of polymer material at the distal end. The idea itself is not new, manufacturers often return to it, and good results have been obtained in single-center studies in terms of reducing reflux nephropathy and irritative symptoms, but such a stent model has not been widely used due to unstable valve operation, impaired passage of drainage contents along the stent, which leads to an increase in the frequency of obstructive complications and does not affect survival patients [13, 14, 54, 64].

Functional disorders on the background of stenting. The problems of functional disorders of the drained organ are even less covered. In the Russian literature, most of the studies devoted to the physiology of the stented ureter are associated with the name of I.S. Mudra [23]. Her work shows the negative impact of both infectious and inflammatory processes and obstruction, as well as the intraluminal location of the stent on electromyographic activity and ureteral peristalsis. Similar conclusions are presented in foreign publications. Thus, in a chronic experiment on a model of a stented native ureter of a pig, an increase in its peristalsis was shown in the first hours after stenting, followed by depression up to the absence of electromyographic activity from the first day of the stent in the ureter [51].

In earlier hydrodynamic studies on the model of the explanted pig organocomplex, it was found that the stent initially causes obstruction, which is caused mainly by a decrease in the extra-laminar flow. Large diameter stents do not violate the latter, i.e. the degree of obstruction correlates with the stent diameter as 27%, 39% and 42% for stents 5, 6, and 7 Ch, respectively [33, 34, 43].

Inflammatory and microcirculatory disorders in the drained segment. An implant of any localization, being a foreign material, causes the development of such a typical pathophysiological process as inflammation. In relation to urinary stents, inflammatory and microcirculatory changes develop in the drained segment, which is accompanied by inflammatory edema and leukocyte infiltration [34, 67].

It is impossible to clearly distinguish the severity of microcirculatory and inflammatory disorders in the stented segment in clinical practice due to the lack of morphological, electromyographic and fluometric monitoring, this requires experimental studies. The degree of inflammatory and microcirculatory disorders is determined by various factors: the bioinertness of the stent material, colonization by microorganisms, the severity of ascending reflux and the addition of stent obstruction, but invariably progresses with increasing drainage time. Prolonged stent placement (more than 4-12 weeks) is accompanied by irreversible sclerotic changes in the wall of the drained organ [26, 33]. The biocompatibility of the stent material should be recognized as the most controlled factor, which is aimed at increasing the main number of studies [19, 34, 67].

Recently, there have been publications concerning the physical characteristics of the stent, which are reflected in the concept of "biomechanical compatibility". The authors point out that achieving the latter can reduce the severity of inflammatory changes in the wall of the drained segment [67, 8].

The analysis of long-term results did not show the advantages of stenting over drainage-free ureteropyeloanastomosis [43]. And although the use of a Double J-stent is recommended for parietal injury of the ureter and after endotomy for stricture of the LMS or ureter [1, 46, 69], we found a report on the formation of a uretero-vaginal fistula 15 days after ureteral stenting in a patient with post-tuberculosis stricture in the upper third against a background of 4-year serological and bacteriological reconvalescence. The cause of such a complication could be trophic disorders in the ureter wall due to the presence of a stent. The patient underwent stent removal and surgical closure of the fistula [65].

Irritative symptoms. The use of Double J-stents in urological practice is associated with the development of irritative symptoms, the frequency of which can reach 35-80% [6, 23, 27]. Dysuria is caused by irritation of the neck of the bladder by the distal curl of the stent. Some hopes were pinned on the use of universal length stents, the thermostable distal end of which is twisted into several curls, which ensures maximum removal from the neck of the bladder. However, a multicenter British study with a sample size of 162 patients did not reveal differences in the severity of stent symptoms in patients with a universal length stent and a Double J stent with a length of 24 cm [49]. Positive results in the form of a decrease in the frequency of irritative symptoms and reflux pyelonephritis were noted during implantation of a jj stent above the vesicoureteral anastomosis. To do this, the authors cut off the vesicular curl from a standard Double J stent [23]. Similar results were observed with the implantation of segmental metal stents Memokath [35, 69]. Single- and multicomponent therapy of stent symptoms with α1-adrenoblockers, M1-cholinolytics, NSAIDs has a positive effect, but does not relieve irritative symptoms [6, 22, 23, 27].

The literature review and analysis of unsolved problems of stenting allow us to substantiate research directions for creating an "ideal" stent with optimal properties.

1. The design solution of the stand and the delivery system should ensure ease of installation and removal of the stent, as well as prevent its migration.

2. Geometric dimensions should contribute to the adequacy of drainage (i.e. minimize the likelihood of obstruction).

3. The mechanical parameters of stents, while maintaining the frame properties, should not increase the risk of microcirculatory disorders in the wall of the drained organ.

4. The stent material should have good bioinert and antiproliferative properties.

5. The stent should not lead to reflux.

6. The surface of the stent should prevent adhesion and replication of bacteria.

7. The stent must have corrosion resistance in biological environments and not precipitate urinary salts.

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