Ureteral JJ Stent – Which One is Better?

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Ureteral stents represent a minimally invasive alternative to preserve urinary drainage whenever the ureter is damaged or is under a significant risk to be occluded due to extrinsic or intrinsic etiology, even due to iatrogenic cause. Ureteral obstruction caused by extrinsic compression is often associated with intra-abdominal neoplasms. The first-line therapy to relieve such obstructions is usually internal drainage with ureteral stents. Ureteral stents made of different materials have been designed to achieve the best drainage possible. In this study, we tried to compare different JJ stent materials – which are better and their pros and cons. The ideal stent that would combine perfect long-term efficacy with no stent-related morbidity is still lacking and stent usage is associated with several adverse effects that limit its value as a tool for long-term urinary drainage. Several new ideas on stent design, composition material and stent coating are currently under evaluation, and are trying to eliminate the drawbacks of ureteral stent usage. Almost every clinician is familiar with the drawbacks that are associated with stents, including infection, encrustation, pain and discomfort.

Keywords: stent, materials, obstruction, composition

Ureteral obstruction caused by extrinsic compression is often associated with intra-abdominal tumors and therefore the internal drainage with ureteral stents is performed to relieve such obstruction. In 1978, *Fineyand Hepperlen* introduced the double-J and single-pigtail stent. Since then the design and composition of the stents were improved and consequently the onset of typical associated complications decreased (i.e. risk of infections, stone deposits on the JJ stent, migration, hyperplastic urothelial reaction, patient's discomfort). Therefore, ideal stent characteristics include, besides the absence of renal impairment, ease of placement and removal, lack of upper and lower tract iritative symptoms and infections, maintenance of an excellent urine flow [1-4].

Current indications for stent placement include relief of ureteral obstruction, whether the cause is intrinsic (from a calculus, clot, or urothelial carcinoma, metastasis) or extrinsic (from external compression or mass effect) [5-12]. Most of these stents are placed for 2-3 weeks, but there are situations that require a longer period up to years. Usually patients with short-term stent placement present pain and discomfort during activity and urination [13], requiring analgesic medication or other types of procedures [14].

Experimental part

Different materials used for ureteral stents

There are three main classes of materials used to fabricate ureteral stents: metals, polymers and bio-degradable/bio-absorbable materials. In comparison to metal stents (introduced by Gort et al.) that are more resistant [15-19], polymeric stents (thermoplastic, thermoset elastomers and silicone-based) are more tolerated by the patients. Bio-degradable/bio-absorbable stents are more recent, and have been shown to reduce the requirement for secondary procedures (i.e. stent removal). The time taken for the stent to be absorbed depends on the material type and potential surface coatings. Dual durometer stents were introduced to decrease bladder irritation.

Stent coating

Stent coating presents many improvements, such as the decrease of biofilm onset, inflammation and also in friction, and consequently lowering the risk of infections and an easier stent passage over a guidewire, too. Specific coatings may also be employed for drug eluting purpose [14]. Numerous strategies have been developed and tested, largely based upon the application of anti-adhesive and antimicrobial compounds.

Heparin

Heparin is a highly-sulfated glycosaminoglycan widely used in medicine for a number of clinical indications, predominantly anticoagulation. Due to its relative safety, high negative charge and existing use as an anti-adhesive coating, the molecule has been applied to urinary stents to reduce biofilm formation and encrustation (Endo-Sof, Radiance, Cook Urological). In addition, this stent has thermosensitive properties that permits softening once exposed to body temperature, increasing the patients' quality of life and comfort.

In 2004, Norbert Laube et al. introduced this type of device for reducing the friction by applying plasma-deposited, diamond-like amorphous carbon material [20].

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In addition, a decrease in biofilm and encrustation formation was proved.

Teflon

Teflon – polytetrafluoroethylene (PTFE) – was discovered by Dr. Roy Plunkett, in 1938. Although it has a wide range of uses (from non-stick frying pans to lubricants or in rocket tanks and telescopes used by NASA), it has been also proved its role in reducing the development of resistant bacteria and biofilm due to the resistance to van der Waals forces and probably also because it is the substance with the lowest coefficient of friction (0.05e0.1) [21,22].

Hydrophilic coatings

Hydrophilic coatings – using polyethylene glycol (PEG) – are another alternative, which act as a deterrent to hydrophobic bacterial surfaces and encrusting deposits within the urine.

Silver

Silver has been widely used as a universal antimicrobial agent for centuries, mainly because of its lack of concomitant host toxicity in comparison to other metal compounds. The exact mechanism is still not fully understood, but data proved its ability to abolish the activity of numerous bacterial enzymes [23].

Chlorhexidine

An Israeli group evaluated C-flex material (Cook Medical, Bloomington, IN) coated with a medical antiseptic (chlorhexidine 1% or 2% as main active compound) inside of a slow release chlorhexidine varnish against *Enterococcus*, *Escherichia,* and *Pseudomonas* in an *in vitro* model, preventing colonization [19]; furthermore, the results showed a stable and controlled release of the antiseptic, maintaining a clean stent [21].

Results and discussion

Stent design

The design of the stent should allow a successfully placement, without consequent migration, and therefore the double-J structure represents the default for almost all other stents. Another important aspect is the stent drainage and, recently, several new features were introduced: side holes, spiral stents, mesh stents, stents with variations in tail designs and the method of the removal. Additionally, the fluidic aspects of stent drainage is an area of interest as different in vitro data showed an association with encrustation and biofilm formation [23].

The Percuflex™ Helical (Boston Scientific) stent is made of the Percuflex™ material. This stent is modified according to the shape of ureter and in this manner it increases the ureteral flexibility without decreasing the urinary flow. The performance of this stent was analyzed by Mucksavage et al. that compared the Helical stent with a control ureter in different situations: an unobstructed ureter, a stented ureter, an extraluminal-obstructed stent and an intraluminale obstructed stent [24,25].

As mentioned above, the most commonly used stent type is the *standard DJS* (double J stent), named due to its J-shaped curled ends. Manufactured from polyurethane, silicone, or various polymers, DJS are changed frequently at approximately 3-6-month intervals, as they are prone to encrustation, obstruction, migration, and fracture [26]. Furthermore, one of the main problems associated with DJS is encrustation of stone formation on the surface of the stent [27]. Polymeric stents have shown to be inferior in long-term drainage when compared to metal stents in the setting of malignant ureteral obstruction.

Gel-based stent

Rosman et al. describe a novel stent that is gel and composed of hydrated, partially hydrolized polyacrylonitrile (pAguaMedicina™ Pediatric UreteralStent (pAMS), Q Urological, Natick, MA); their findings were encouraging for the decrease of bacterial adherence (up to 70%). Biofilm formation was still present, but the time to accumulation was prolonged compared to the control stent. In conclusion, this stent can reduce the risks of infections [27].

Metallic stents represent a good alternative. Different types of metallic stents exist: non-expandable coiled metallic Resonance stent (Cook Medical, Bloomington, IN, USA), thermo-expandable metal alloy Memokath 051 stent (PNN Medical, Glostrup, Denmark), and self-expandable covered metallic UVENTA stent (Taewoong Medical, Gojeong-ro, Wolgot-myeon, Gimposi, Gyeonggi-do, South Korea) [28].

The Resonance® stent was initially developed by CookUrological for malignant ureteral obstruction; the stent is composed of a tightly coiled wire made of nickel-cobalt-chromium-molybdenum alloy. Partially, it looks like a *double-J* stents, but its ends are occluded. The novelty of this stent is that it is MRI (magnetic resonance imaging)-compatible [20]. A study by Christman et al. showed that Resonance stent can maintain 50% diameter with over 31 lb. of compression force placed on its proximal, mid, and distal portions [29].

Another type of ureteral stent is *UVENTA* stent, made of two layers of a self-expandable nickel-titanium alloy mesh covering a polytetrafluoroethylene (PTFE) layer. The outer mesh containing a nickel-titanium skeleton prevents stent migration. The inner PTFE and mesh layers prevent tissue ingrowth and maintain stent patency [30].

Metallic stents versus plastic double J stents

Chow et al. study highlighted an increase in functional duration of 4 months using the Resonance stent when comparing to a regular polymeric stent in patients with MUO (malignant ureteral obstruction). Hydronephrosis and serum creatinine subsided or remained the same in 90% of these patients and the stent duration was not affected by severe hydronephrosis. In conclusion, the Resonance stent was more effective in cases with severe obstruction. Only minor complications were reported (dysuria, fever, urinary frequency, flank pain, and hematuria), similar to those seen with the polymeric stents [31].

Chung et al. compared the UVENTA stent (in 32 patients) to the standard polymeric DJS (in 56 cases). Both stents were placed for MUOs caused by various cancers and only minor complications were noticed in both groups – mild pain, hematuria, and UTIs (urinary tract infections). Stent migration only occurred in one UVENTA patient. In terms of patency (defined as the time between the initial insertion and secondary procedure to ensure there was urinary drainage) and technical success, the UVENTA stent was superior to DJS. This study proved that the UVENTA stent was safe and effective in palliative treatment of MUO [32,33].

Biodegradable ureteral stents

One of the most recent discoveries is the biodegradable ureteral stent that can eliminate the related stent risks, and also the removal procedure and chronic indwelling stents complications (encrustation, stone formation, infection). The forgotten stent is a common complication feared by urologists, as it has been associated with potential kidney loss, and even death.

In 2008, a study performed *in vivo* on a porcine model compared drainage, degree of hydronephrosis, ureteral dilatation, and urinary tract infection risks between a

degradable L-glycolic acid (Uriprene™, Poly-Med Inc., Anderson, SC) stent and a standard stent. The results showed that the Uriprene stents began to degrade at 3 weeks and completely in 10 weeks. Additionally, this new stent presented less ureteral dilatation and fewer infections events. The main problems of this stent were the long period of degrading (7-10 weeks) and that the axial rigidity was too soft (consequently, it presented difficulties in advancing the stent directly over a guidewire) [34,35].

A second generation was developed to degrade faster and the Chew et al. study [33,34] presented satisfying results: improved axial rigidity, and 80% of stents degraded over 2-3 weeks and completely by week 4 [20,35].

Ureteral stent development is currently focusing on the enhancement and evolution of stent design, composition material and stent coating. The results are promising and, hopefully, in the near future new stents will be introduced for the management of a growing variety of new indications, with decreased onset of the related stent risks. Every type of ureteral stent has its advantages and disadvantages. Research and development of ureteral stents require an extensive understanding of the mechanisms involved in ureteral stent failure, especially in patients with several comorbidities (e.g. chronic kidney disease, diabetes mellitus, malnutrition etc.) [36-38]. Urothelial hyperplasia, stent biofilm formation and encrustation, ureteral mobility and response to ureteral intraluminal foreign-body stimuli still represents major complications that are not fully understood.

Conclusions

Although the perfect ureteral stent does not exist, the devices continue to improve. Currently, technological innovations are focusing on the enhancement and evolution of stent design, material composition and surface coatings. Ultimately, success may lie in the development of multiple devices, each with its own clinical target, or in one device that is able to simultaneously incorporate multiple strategies that can work in synergy.

References

1.ISVORANU, I., PERIDE, I., RADULESCU, D., NICULAE, A., SINESCU, R.D., CHECHERITA, I.A., Rev. Chim.(Bucharest), **66**, no. 9, 2015, p. 1316

2.ISVORANU, I., RADULESCU, D., PERIDE, I., NICULAE, A., SINESCU, R.D., CHECHERITA, I.A., Rev. Chim.(Bucharest), **66**, no. 8, 2015, p. 1239

3.CHECHERITA, I.A., DAVID, C., CIOCALTEU, A., LASCAR, I., Chirurgia (Bucur.), **104**, nr. 5, 2009, p. 525

4.MITOIU, D., DAVID, C., PERIDE, I., NICULAE, A., MURESAN, A., CIOCALTEU, A., GEAVLETE, B.F., CHECHERITA, I.A., Rom. J. Morphol. Embryol., **55**, nr. 4, 2014, p. 1409

5.GEAVLETE, B.F., BRINZEA, A., CHECHERITA, I.A., ZURAC, S.A., GEORGESCU, D.A., BASTIAN, A.E., ENE, C.V., BULAI, C.A., GEAVLETE, D.O., ZAHARIA, M.R., GEAVLETE, P.A., Rom. J. Morphol. Embryol., **56**, nr. 3, 2015, p.1069

6.GHEORGHISAN-GALATEANU, A., TERZEA, D.C., CARSOTE, M., POIANA, C., J. Ovarian Res., **6**, nr. 1, 2013, p. 28

7.POIANA, C., NEAMTU, M.C., AVRAMESCU, E.T., CARSOTE, M., TRIFANESCU, R., TERZEA, D., NEAMTU, O.M., FERECHIDE, D., DANCIULESCU MIULESCU, R., Rom. J. Morphol. Embryol., **54**, nr. 3 Suppl, 2013, p. 717

8.CARSOTE, M., PAUN, S., NEAMTU, M.C., AVRAMESCU, E.T., IOSIF, C., TERZEA, D., CONSTANTINOIU, S., DANCIULESCU MIULESCU, R., NEAMTU, O.M., POIANA, C., Rom. J. Morphol. Embryol., **53**, nr. 2, 2012, p. 401

9.MARCU, R.D., SPINU, A.D., SOCEA, B., BODEAN, M.O., DIACONU, C.C., VASILESCU, F., NEAGU, T.P., BRATU, O.G., Rev. Chim.(Bucharest), **69**, no. 4, 2018, p.823

10.PAUN, D.L., POIANA, C., PETRIS, R., RADIAN, S., MIULESCU, R.D., CONSTANTINESCU, G., ORBAN, C., Chirurgia (Bucur.), **108**, nr. 6, 2013, p. 900

11.NEAGU, T.P., TIGLIS, M., BOTEZATU, D., ENACHE, V., COBILINSCHI, C.O., VALCEA-PRECUP, M.S., GRINTESCU, I.M., Rom. J. Morphol. Embryol., **58**, nr. 1, 2017, p. 33

12.NEAGU, T.P., SINESCU, R.D., ENACHE, V., ACHIM, S.C., TIGLIS, M.I., MIREA, L.E., Rom. J. Morphol. Embryol., **58**, nr. 2, 2017, p. 603

13.YANG, L., WHITESIDE, S., CADIEUX, P.A., DENSTEDT, J.D., Asian J. Urol., **2**, nr. 4, 2015, p. 194

14.NEAGU, T.P., COCOLOS, I., COBILINSCHI, C., TIGLIS, M., FLORESCU, I.P., BADILA, E., SINESCU, R.D., Rev. Chim.(Bucharest), **68**, no. 12, 2017, p. 2978

15.MOSAYYEBI, A., VIJAYAKUMAR, A., YUE, Q.Y., BRES-NIEWADA, E., MANES, C., CARUGO, D., SOMANI, B.K., Cent. European J. Urol., 2017, **70**, nr. 3, p. 270

16.MARDIS, H.K., KROEGER, R.M., MORTON, J.J., DONOVAN, J.M., J. Endourol., 1993, **7**, nr. 2, p. 105

17.HOFMANN, R., HARTUNG, R., World J. Urol., 1989, **7**, nr. 3,p. 154

18.ABRAMS, H.L., Abrams' angiography: interventional radiology: Lippincott Williams & Wilkins, 2006

19.LAUBE, N., http://www.eurekalert.org/pub_releases/2004-11/uob-daa111804.php

20.BROTHERHOOD, H., LANGE, D., CHEW, B.H., Transl. Androl. Urol., **3**, nr. 3, 2014, p. 314

21.LOPEZ-LOPEZ, G., PASCUAL, A., PEREA, E.J., J. Med. Microbiol., **34**, nr. 6, 1991, p. 349

22.ELAYARAJAH, B., RAJENDRAN, R., VENKATRAJAH, B., SREEKUMAR, S., SASUDHAKAR, JANIGA, P.K., Int. J. Eng. Sci. Technol., **3**, nr. 1, 2011, p. 544

23.SLAWSON, R.M., VAN DYKE, M.I., LEE, H., TREVORS, J.T., Plasmid., **27**, nr. 1, 1992, p. 72

24.CHEW, B.H., KNUDSEN, B.E., NOTT, L., PAUTLER, S.E., RAZVI, H., AMANN, J., DENSTEDT, J.D., J. Endourol., **21**, nr. 9, 2007, p. 1069

25.MUCKSAVAGE, P., PICK, D., HAYDEL, D., ETAFY, M., KERBL, D.C., LEE, J.Y., ORTIZ-VANDERDYS, C., SALEH, F., OLAMENDI, S., LOUIE, M.K., MCDOUGALL, E.M., Urology, **79**, nr. 3, 2012, p. 733

26.CHUNG, H.H., KIM, M.D., WON, J.Y., WON, J.H., CHO, S.B., SEO, T.S., PARK, S.W., KANG, B.C., Cardiovasc. Interv. Radiol., **37**, nr.2, 2013, p. 463

27.PAVLOVIC, K., LANGE, D., CHEW, B.H., Asian J. Urol., **3**, nr. 3, 2016, p. 142

28.ROSMAN, B.M., BARBOSA, J.A., PASSEROTTI, C.P., CENDRON, M., NGUYEN, H.T., Int. Urol. Nephrol., **46**, nr. 6, 2014, p. 1053

29.CHRISTMAN, M.S., L'ESPERANCE, J.O., CHOE, C.H., STROUP, S.P., AUGE, B.K., J. Urol., **181**, nr. 1, 2009, p. 392

30.KIM, K.S., CHOI, S., CHOI, Y.S., BAE, W.J., HONG, S.H., LEE, J.Y., KIM, S.W., HWANG, T.K., CHO, H.J., J. Laparoendosc. Adv. Surg. Tech. A., **24**, nr. 8, 2014, p. 550

31.CHOW, P.M., CHIANG, I.N., CHEN, C.Y., HUANG, K.H., HSU, J.S., WANG, S.M., LEE, Y.J., YU, H.J., PU, Y.S., HUANG, C.Y., PLoS One, **10**, nr. 8, 2015, e0135566

32.CHUNG, H.H., KIM, M.D., WON, J.Y., WON, J.H., CHO, S.B., SEO, T.S., PARK, S.W., KANG, B.C., Cardiovasc. Interv. Radiol., **37**, nr. 2, 2014, p. 463

33.CHUNG, K.J., PARK, B.H., PARK, B., LEE, J.H., KIM, W.J., BAEK, M., HAN, D.H., J. Endourol., **27**, nr. 7, 2013, p. 930

34.CHEW, B.H., PATERSON, R.F., CLINKSCALES, K.W., LEVINE, B.S., SHALABY, S.W., LANGE, D., J. Urol., **189**, nr. 2, 2013, p. 719

35.CHEW, B.H., LANGE, D., PATERSON, R.F., HENDLIN, K., MONGA, M., CLINKSCALES, K.W., SHALABY, S.W., HADASCHIK, B.A., J. Urol., **183**, nr. 2, 2010, p. 765

36.NICULAE, A., JINGA, M., CIOCALTEU, A., LASCAR, I., JINGA, V., CHECHERITA, I.A., Rom. J. Morphol. Embryol., **52**, nr. 3, 2011, p. 863

37.NICULAE, A., DAVID, C., DRAGOMIRESCU, R.F.I., PERIDE, I., TURCU, F.L., PETCU, L.C., COVIC, A., CHECHERITA, I.A., Rev. Chim.(Bucharest), **68**, no. 2, 2017, p. 354

38.MANDA, G., CHECHERITA, A.I., COMANESCU, M.V., HINESCU, M.E., Mediators Inflamm., **2015**, 2015, p. 604208

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