Metallic Double Pigtail Ureteral Stent Usage During Extracorporeal Shock Wave Lithotripsy in the Swine Model: Is There Any Effect on the Ureter?

Evangelos N. Liatsikos, M.D., Ph.D.,1 Panagiotis Kallidonis, M.D.,1 Iason Kyriazis, M.D.,1 Dimitrios Karnabatidis, M.D., Ph.D.,2 Athanasios Tsamandas, M.D., Ph.D.,3 George Sakellaropoulos, Ph.D.,4 Nicolaos Flaris, M.D., Ph.D.,5 Christos Rigopoulos, M.D.,1 Charalambos Toronidis, M.D.,1 Ioannis Efthimiou, M.D.,1 Kriton Filos, M.D., Ph.D.,5 Dimitrios Siablis, M.D., Ph.D.,2 and Petros Perimenis, M.D., Ph.D.1

Abstract

Purpose: To examine the safety and compatibility of full-length metal ureteral stent usage with extracorporeal shock wave lithotripsy (SWL).

Methods: Four Resonance™C212 ureteral stents and four special Resonance ureteral stents modified to contain thermocouples were placed unilaterally in eight pigs, with contralateral ureter of each pig serving as its own control. All pigs were subjected to the same SWL protocol in both their ureters. In the animals containing the modified stents, ureter temperature was monitored during treatment. The animals were sacrificed on days 1 and 15 after treatment, and both their ureters were histologically examined.

Results: No statistically significant increase (mean increase of 0.5 ± 8°C, p > 0.05) of stent temperature was observed during treatment. No differences in histology were observed among ureters containing stents and control ureters at both days 1 and 15 after treatment.

Conclusion: SWL appears to be harmless for the ipsilateral ureter.

Introduction

FULL-METAL DOUBLE pigtail ureteral Resonance™ stent (RS) (Cook Urological, Limerick, Ireland) presents a promising long-term option for the management of malignant extrinsic ureteral obstruction. Its incompressible structure provides the potential to preserve ureteral flow in cases where percutaneous nephrostomy is the only option.1–3 Despite limited clinical experience worldwide with this novel stent, the existing reports reveal stent encrustation in several cases.2,3 Unpublished data of the usage of this nickel–cobalt–chromium–molybdenum alloy stent from our department verified the generation of calcium phosphate and oxalate encrustation around the stent at approximately 1 year after stent insertion, resulting in stent removal. A characteristic case of an RS indwelling for 14 months that was carrying heavy encrustation on its surface is presented in Figure 1. Despite the formation of encrustation on RSs, excellent drainage was present in most of the cases throughout the treatment. Considering the above, we designed an experimental study for the evaluation of compatibility of ureteral metal stent usage with extracorporeal shock wave lithotripsy (SWL) in an attempt to provide data on the safety of managing formed encrustations or even stones via SWL and consequently avoiding stent replacement.

The effect of SWL on stented with RS ureters was evaluated through histologic examination. The pathological evaluation was selected as the most appropriate method to verify any injury due to treatment or stent placement. Moreover, the chord-like metal structure of RS revealed the possibility that its vibration due to SWL might cause temperature increase and subsequent thermal injury to the ipsilateral ureter. Although temperature increase and thermal injury during SWL treatment have never been reported, the above assumption led us to examine the thermal behavior of RS during SWL treatment.

Materials and Methods

Animals and anesthesia

Eight domestic pigs weighing between 20 and 25 kg were studied. The protocol was approved by the Institutional Departments of 1Urology, 2Radiology, 3Pathology, 4Basic Medical Science, and 5Anesthesiology and Intensive Care, University of Patras, Patras, Greece.
Animal Care Committee of our institution. All animals were allowed 72 hours minimum before the procedure to recover from the stress of transportation. Food and water was withheld for 12 hours before anesthesia. All interventions were performed in standard operating room equipped with C-arm fluoroscope and extracorporeal shock wave lithotripter with the animals under general anesthesia.

The animals were anesthetized using a combination of ketamine, xylazine, and atropine sulfate. The pigs were then intubated and ventilated. Intravenous propofol 5% was used to maintain anesthesia for the whole duration of the procedure. Postoperative analgesia was achieved by intramuscular administration of morphine sulfate when indicated. Prophylactic, perioperative, and postoperative antibiotics were administered to all animals.

**Ureteral catheters**

Under fluoroscopic guidance, four kinds of ureteral catheters were introduced to the subjects via cystoscopy. The original double pigtail RS (n = 4); an original double pigtail catheter (C-Flex®, Cook Urological) (n = 2); a modified Resonance stent containing three thermocouples in its distal, middle, and proximal portions (n = 4); and a modified ureteral catheter (C-Flex®, Cook Urological) containing two thermocouples in its distal and proximal portions as well (n = 2).

Omega Precision Fine Wire Thermocouples (Omega Engineering, Stamford, Connecticut) were used in this experiment. Each thermocouple was constituted by a single wire that is looped and encased in two plastic sheaths. The distal end of the thermocouple was looped and continuous, and it was this end where temperature was measured. At the proximal end of each thermocouple, the plastic sheaths were separated and connected to the appropriate data logger device. For the creation of the thermocoupled RS, a modified version of the RS without the pigtail design was used. The modification was deemed necessary given that it was impossible to attach thermocouples to a standard RS. The modified silicone ureteral catheters were created by inserting the thermocouples inside their lumen, letting their distal ends exit the lumen through tiny holes created to the catheter (Fig. 2).

**Catheter placement**

Each pig was placed in the supine position, and a 0.035-inch hydrophilic guidewire was placed bilaterally in each ureter via cystoscopy. The pigs were separated into four groups. Group 1 included two pigs carrying a modified ureteral catheter (with thermocouples) in the right ureter and a modified RS in the left ureter. Group 2 (n = 2) had only modified RSs in the left ureter. Group 3 included pigs with double pigtail stents in the right ureter and RS in the left one. Pigs carrying only RS were defined as Group 4. Details of catheters and stents placed in each pig are given in Table 1. In the right ureter of two pigs, a 6F ureteral catheter was introduced under fluoroscopic guidance and positioned in the renal pelvis. These two catheters were carrying thermocouples. In two more pigs, double pigtail catheters were inserted in the right ureter. In the remaining four pigs, the right ureter remained intact without stenting and served as control. The guidewire was then removed from the right ureter under fluoroscopic control. In the left ureter of all animals (n = 8), a 5F/9F catheter/sheath system was placed over the guidewire and introduced in the renal pelvis under fluoroscopic control. The 5F catheter and the guidewire were removed leaving the 9F sheath in place. A 6F Resonance metal stent was inserted in the renal pelvis through the 9F introducer sheath, and then the sheath was removed, allowing the distal coil of the stent to form in the bladder. Four of these RSs were modified to contain thermocouples.

**SWL protocol**

A Dornier Lithotripter SII was used. Bilateral SWL (3200 shock waves, 70% intensity, and 120 trigger rate) was performed targeting the upper third of each ureter (Fig. 3).

**Temperature measurement**

During treatment, temperature was measured every 2 seconds by each thermocouple and saved by a data logger device (DX106; Yokogawa Europe, Amersfoort, The Netherlands). The latter device was a six-channel data logger, and each thermocouple was connected to one of the channels.

The correct function of the thermocouples was evaluated before, during, and after the SWL treatment. Thermocouple measurements obtained before and after usage should demonstrate the room temperature. During the session, the temperature measurements in damaged thermocouples showed meaningless information ranging between 0 and 2500°C. Measurements obtained from thermocouples that could be considered unreliable were excluded from the analysis. During our experiment, only one thermocouple was identified to be damaged, and was removed.

**Ureter removal**

One day after the procedure, the pigs carrying the modified stents with the thermocouples (n = 4) were sacrificed using high doses of anesthesia, and both their ureters were resected for histological examination. The first postoperative day for the sacrifice of the above pigs was deemed necessary in an effort to study the acute effects of the combination of SWL...
with stents containing thermocouples. Moreover, the animals could not tolerate the protruding catheters postoperatively. Fifteen days later, the remaining four animals were sacrificed, and their ureters were histologically examined to elucidate the mid-term histological effects of the applied treatment. Pathological examination was blinded and performed by the same pathologist in an effort to minimize possible bias.

Statistical analysis
Linear regression analysis was performed to check whether the rate of temperature increase was similar in different parts of the stent throughout the experiment. One-way analysis of variance was performed in data derived from each catheter to check whether there was any significant difference between temperatures of the proximal, middle, or distal parts of the stent at each time point. Finally, t-test was performed to examine whether starting stent temperature was significantly different from the stent temperature at the end of the experiment. The threshold of statistical significance was set at 5% ($p = 0.05$).

Results
All stents were successfully positioned, and the perioperative course was uneventful. No complications were encountered during the 15 days after the operation.

Temperature measurements
No statistically significant difference between the temperatures of the upper, middle, and lower parts of RS was observed ($p > 0.05$). No statistically significant difference between the temperatures of the upper and lower parts of ureteral catheter was noted either ($p > 0.05$). A nonstatistically significant increase of RS temperature along its length was observed during the whole duration of the experiment.
mean starting temperature was 37.5°C, and peak temperature at the end of the experiment was 38°C (SD = 0.8, p > 0.05). A nonstatistically significant increase of ureteral catheter temperature along its length was observed as well; mean starting temperature was 37.3°C, and peak temperature at the end of the experiment was 37.5°C (SD = 0.7, p > 0.05) (Fig. 4). Temperature elevation rate was not different in any part of the RS or ureteral catheter (p > 0.05).

**Ureteral histology**

Histological features observed in the resected ureters were minimal chronic inflammation and mild glandular metaplasia. No epithelial denudation was observed in any of the ureters. No histological differences between left and right (control) ureters were observed on days 1 and 15 after treatment in all eight experimental subjects (Fig. 5).

**Discussion**

After the use of metal mesh stents (MS) in the cardiovascular and biliary system, their use was expanded with promising results in the urinary tract.4–9 MS have been used to manage urethral strictures, benign prostatic hyperplasia, detrusor-sphincter dyssynergia, and ureteral obstruction.4–9 Our experience and the experience of other groups include the use of MS for the management of malignant ureteral obstruction, ureteroileal anastomotic strictures, ureteropelvic junction obstruction, and kidney transplantation.7–14 Nevertheless, the application of MS in the urinary tract has been related with several complications; more prominent is the urothelial hyperplasia through the stent struts, stent migration, and encrustation.5,6,9,10,15 More recently, drug-eluting stents have been proposed for the management of urothelial hyperplasia, but the migration and encrustation problems have not yet been addressed directly.16

![FIG. 3. Pulse fluoroscopy of porcine abdomen before the beginning of shock wave lithotripsy. A target of the upper third of the ureter was chosen to be treated in all animals.](image)

![FIG. 4. (A) Mean values of temperatures at each time point, from all four animals wearing modified RS with thermocouples during SWL. Temperature of the upper, middle, and lower segments of RS is demonstrated separately. (B) Mean values of temperatures at each time point, from both animals wearing modified silicone catheter with thermocouples during SWL. Temperature of the upper and lower segments of catheter is demonstrated separately. Standard errors for each value have been removed. RS = Resonance stent; SWL = shock wave lithotripsy.](image)
Nevertheless, experience reported with the RS is limited. Borin et al\textsuperscript{1} were the first to report the use of the stent for relieving intractable ureteral obstruction due to retroperitoneal fibrosis secondary to breast cancer. Wah et al\textsuperscript{2} reported clinical data on malignant ureteral obstruction in 15 patients managed by RS. The authors concluded that the all-metallic pigtail stent might be adequate for long-term urinary drainage of malignant ureteral obstruction without concomitant bulky pelvic disease. Moreover, Nagele et al\textsuperscript{3} managed 18 collecting systems (14 patients) with both benign and malignant disease with good results. The mean follow-up period was 8.6 months, and observed encrustation was reported in two stents. Seven stents were removed due to persistent hematuria, severe dysuria, pain, and insufficient drainage. The proper stent length was considered mandatory for patient comfort.\textsuperscript{3}

An experimental study by Blascko et al\textsuperscript{17} compared the RS with a standard ureteral stent and reported that the Resonance provides less overall flow than standard stent. Nevertheless, extrinsic compression sufficient to occlude a standard stent did not affect the metal stent that provided satisfactory drainage.\textsuperscript{17}

The observation of stent encrustation during our clinical experience with the RS led us in considering SWL as a therapeutic modality in urinary stone disease in patients carrying RS, especially in the case of patients with benign obstructive diseases. FIG. 5. Histological features of both right and left ureters on day 15 (subject no 7). (A, B) Photomicrographs showing a section from the right ureter that was blank during treatment and served as control. There is mild focal glandular metaplasia (black arrows) and minimal chronic inflammation (green arrows). (C, D) Photomicrographs showing a section from the left ureter that contained an RS during treatment. Changes are similar to those observed in the right ureter. There is mild focal glandular metaplasia (black arrows) and minimal chronic inflammation (green arrows) [hematoxylin–eosin; (A, C) \texttimes20 and (B, D) \texttimes400]. RS = Resonance stent.
disease. A hypothesis has been proposed that due to the chord-like metal structure of RS, SWL of the ureter containing the stent would be related with RS vibration and potentially with an increase in catheter temperature. In the current study, the data do not verify an increase of stent temperature caused by SWL. A slight rise in stent temperature was noted in all stents subjected to SWL; however, it was not statistically significant and did not cause histological deterioration to the ipsilateral ureter. It should be noted that stent temperature never increased more than 0.5°C throughout the procedure in the four pigs bearing the modified stents. Despite the fact that the SWL protocol is customized according to each clinical case, we do not have reasons to believe that temperature elevation would have been higher in humans. Moreover, the SWL protocol of the current experiment was chosen to follow one of the most intensive scenarios.

Two potential mechanisms of ureteral injury during SWL of stented ureters were examined in the current study. It has been assumed that SWL causes vibration to RS by the transformation of the shock wave energy into mechanical energy and fluttering of the stent. Friction between stent vibration and ureter epithelium might be related with urothelial damage. The second mechanism proposes that stent vibration might cause friction between the adjacent metallic coils of RS and might transform a part of this energy into heat. If this increase was sufficient enough, thermal injury to the ureteral epithelium might occur.

The current study provides data that indicate that either friction of the stent in the ureter does not occur or it is harmless for the ureter. Friction of RS with the ureter would have been obvious as epithelial denudation in the histological samples, which is the mildest superficial epithelial damage usually caused by manipulation of metal structures inside the ureter (e.g., catheter insertion). In terms of stent temperature, no significant temperature increase was noted.

It should be noted that the current experimental protocol was designed so that the results of the ureters containing modified RSs could be directly compared with modified ureteral catheters carrying thermocouples (Group 1). Thus, the temperature variation could be studied bilaterally simultaneously in the same animal. Group 2 configuration evaluated possible influence of the modified stent or SWL in the histology of the specimens. These animals (Groups 1 and 2) were sacrificed the first postoperative day, and the acute effect could be evaluated. Moreover, to reveal any late effects, the rest of the animals with the RSs on the right ureter and a double pigtail or no catheter at all in the left ureter were sacrificed at 15 days postoperatively (Groups 3 and 4). The latter configurations were chosen to elucidate any effect of the stent itself in the histology of the specimens.

It could be advocated that the urine flow through the ureter might influence the temperature measurement because urine is a good conductor of heat. The conditions of experiment eliminate the latter possibility. Water was withheld from the studied animals 12 hours before the procedure, and the urine output was not expected to be high. Moreover, the temperature variation was uniform in all subjects—a fact that demonstrates that the urine flow influence on ureteral temperature during the experiment is not significant. Finally, the performance of SWL in humans is tested in the presence of urine flow, and as a result the current experiment simulates the clinical conditions.

Both acute and mid-term histological examinations of ureters containing RS during SWL demonstrated no differences between studied and control ureters. As a consequence, SWL could be considered safe for the ipsilateral ureter. However, all stents used in the current study were free of encrustation and previously formed stones. Consequently, the promising results on the safety of SWL in ureters carrying RSs remain to be verified in clinical trials.

**Conclusion**

No significant temperature elevation and histological deterioration was observed when porcine ureters containing RSs were subjected to SWL. Clinical trials are deemed necessary to further investigate and verify the aforementioned experimental data on the safety and compatibility of SWL with Resonance full-metal stents in human patients.

**Disclosure Statement**

No competing financial interests exist.

**References**


Abbreviations Used
MS = mesh stents
RS = Resonance stent
SWL = shock wave lithotripsy