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First Prize

Impact of a Double-Pigtail Stent on Ureteral Peristalsis in the Porcine Model: Initial Studies Using a Novel Implantable Magnetic Sensor

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ABSTRACT

Background and Purpose: The effect of stents on ureteral peristalsis *in vivo* is not entirely clear. We sought to develop a minimally invasive method for its study.

Materials and Methods: In female domestic pigs, electrical potentials from the ureter were measured by bipolar steel-wire electromyography electrodes delivered laparoscopically. Mechanical movement was measured by giant magneto resistive sensors mounted on custom-made aluminum strips. After baseline values were obtained, the animals were randomized to receive silicone or polyurethane stents, and ureteral peristalsis was measured for 8 hours acutely and for 4 hours 1 week later.

Results: Implantation of the devices took an average of 30 minutes. A consistent correlation was found between laparoscopically observed peristaltic waves and the peristalsis detected by the two measuring devices. The devices themselves did not affect peristalsis. Stent insertion increased peristaltic activity initially but later reduced or stopped it. There was no difference in the effects of the two types of stents.

Conclusions: The new technique permits close monitoring of ureteral peristalsis *in vivo*. Smaller stents appear to have less immediate effect than larger ones, but all type of stents tested eventually caused aperistalsis.

INTRODUCTION

DESPITE THE CLINICAL APPLICATION of the double-pigtail stent for more than two decades since its introduction by Finney in 1978,¹ the clinical role and value of ureteral stenting remain controversial. This is partly attributable to the lack of an accurate and reliable method of studying ureteral pathophysiological activity in a stented system. There are few reported studies on the effects of indwelling ureteral stents on ureteral peristalsis.²⁻⁷ *In vitro* studies measuring the ureteral smooth-muscle activity have had limited clinical applicability

because of the difficulty in correlating evaluations of *in vitro* models with an intact *in vivo* ureter.

Studies to evaluate ureteral peristalsis have largely used endoluminal methods: an ultrasound probe or pressure transducer has been deployed inside the ureter. However, these endoluminal devices can themselves alter ureteral peristalsis, and, hence, intraluminal evaluation technologies cannot accurately define ureteral peristalsis and the ureter's response to stenting.² As such, we searched for an extraluminal method to better study peristalsis in the stented ureter and to compare that with an unstented ureter. Previously, application of an extraluminal

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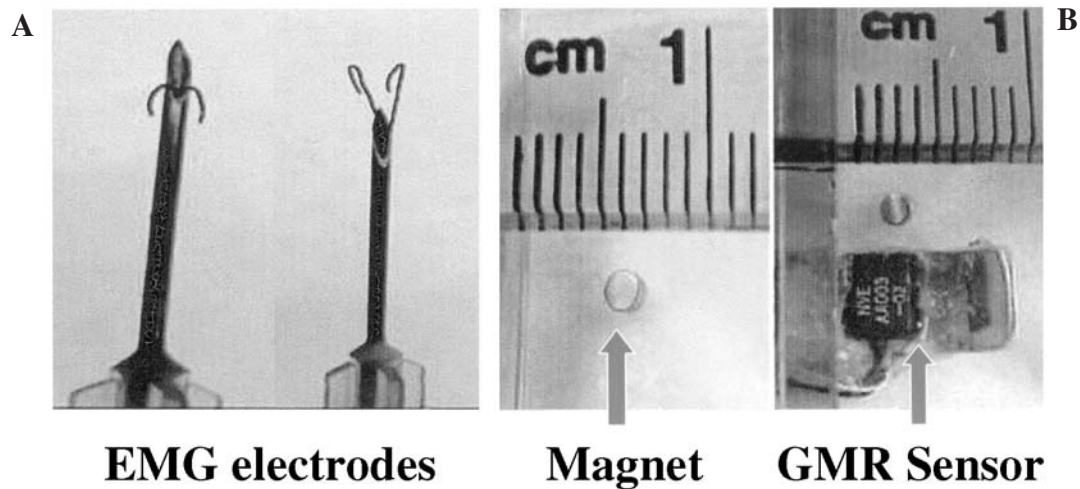


FIG. 1. Experimental equipment. (A) Bipolar EMG wire electrodes mounted on hypodermic needle. (B) Neodymium magnetic disc and GMR sensor.

method using a strain gauge on the surface of the ureter has been reported to study peristalsis.⁸ However, in our experience, the use of strain gauge technology for this purpose is tedious, difficult, and imprecise.

Accordingly, we sought to study ureteral peristalsis by developing a novel minimally invasive extraluminal method using a diminutive magnetic sensor that could be deployed laparoscopically. Placement of this giant magneto resistive (GMR) sensor results in minimal disturbance of the ureteral anatomy. In addition, we studied simultaneously the electrical component of ureteral peristalsis using electromyography (EMG) leads and recorded endoscopic observations of ureteral peristalsis. After establishing the consistency of the magnetic sensor in detecting motility in the normal ureter, the acute effect of indwelling double-pigtail stents on ureteral peristalsis was evaluated. Two types of stents (silicone or polyurethane based) and two sizes (4.7F and 7F) were used.

The purpose of the present study was twofold. First, we sought to design an efficient and reliable minimally invasive extraluminal method to study ureteral peristalsis. Second, with this model, we wanted to evaluate the acute and chronic effects of indwelling ureteral stents of different sizes and compositions on ureteral motility.

MATERIALS AND METHODS

Materials

All investigation was performed with permission from the Washington University School of Medicine Animal Studies Committee. Twenty-two female domestic pigs 4 to 5 months of age weighing 28 to 30 kg were used to study the acute effects of different types of double-pigtail stents.

The electrical potentials from ureteral peristalsis were measured by two sets of modified bipolar steel-wire EMG electrodes. The electrodes were mounted on a 21-gauge, 0.75-inch hypodermic needle (Fig. 1A) to facilitate laparoscopic deployment on the serosal surface of the ureter. The Teflon-coated

wires from both electrodes led to two multipin connectors. The EMG signals from the electrodes were amplified and displayed on a multichannel oscilloscope.

The mechanical movement of ureteral peristalsis was measured by the GMR sensor. The technology consists of a small neodymium disc that creates a magnetic field and a GMR sensor (NVE, Inc., Eden Prairie, MN) that identifies any changes in the magnetic field produced by movement of an object within the field. The magnet and the GMR sensor are very sensitive and small, measuring 2×0.5 mm and $4 \times 4 \times 0.75$ mm, respectively (Fig. 1B). The GMR sensor was mounted on a custom-made aluminum strip for ease of laparoscopic deployment and for accurate positioning under the ureter (Fig. 2). The sensor uses a Wheatstone bridge circuit, and the signals from the sensor were amplified and displayed simultaneously on the

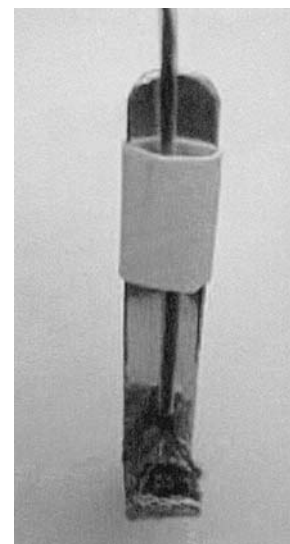


FIG. 2. GMR sensor mounted on aluminum strip for laparoscopic deployment and placement under ureter.

same oscilloscope as the EMG signals (Fig. 3). This unique sensor and its method of placement were developed in our laboratory over an 8-month period.

Methods

After a 16-hour fast (but no fluid restriction), the pigs were anesthetized using xylazine, 0.45 mg/kg, and intubated and ventilated using isoflurane anesthesia at a constant concentration of 2%. Intravenous yohimbine was used to reverse the effects of xylazine soon after the insertion of the trocars. Ketamine and atropine were not used because of their known significant effects on ureteral peristalsis. The pig was placed in a lateral decubitus position, and, using a three-port laparoscopic technique, the ureter was identified without any dissection. The peritoneum overlying the upper and mid ureter was gently reflected medially to expose the surface of the ureter. The pig was hydrated with 5% glucose–0.5N saline at a constant intravenous infusion rate of 5 mL/kg of body weight. Pneumoperitoneum pressure was maintained between 6 and 8 mm Hg to minimize the physiological effects of pneumoperitoneum. The urine output was monitored through a Foley catheter, which was clamped and unclamped every hour to closely mimic normal physiologic bladder filling and emptying. Preoperatively, serum creatinine measurement and a urine culture were obtained.

After exposure of the ureter, the baseline peristaltic rate and frequency were documented by laparoscopic visual observation. Next, the EMG electrodes and the magnetic sensor were deployed laparoscopically. The first set of electrodes was placed under the adventitia of the ureter about 3 cm distal to the ureteropelvic junction, with the hooks of the electrode wire facing the muscular surface. Electrode positioning was achieved by inserting the electrode needle through the adventitia and retracting the needle back over the wires, leaving the tips of the wire electrodes on the ureteral surface. The second set of electrodes was placed about 6 to 7 cm distal to the first set.

A small window (<1 cm) was created under the ureter for placement of the magnet and the magnetic sensor between the two sets of EMG electrodes (Fig. 4). Care was taken to maximally preserve the ureteral blood supply. The above arrangement of EMG leads provided good correlation of endoscopically visible propagative peristaltic waves.

To deploy the GMR sensor, the small magnetic disc was mounted on an applicator using K-Y jelly to keep it adherent to the applicator tip. The magnetic surface was coated with a thin layer of fibrin glue and deployed on the anterior surface of the ureter. The sensor was positioned under the posterior surface of the ureter opposite the magnet. As the peristaltic wave propagates along the ureter, the magnet on the ureteral surface moves in relation to the sensor, and this movement produces a change in the magnetic field, which is picked up by the GMR magnetic sensor.

Baseline peristalsis was measured for 30 minutes before and 30 minutes after the deployment of the EMG and magnetic sensor devices. The EMG and magnetic sensor signals were continuously monitored for 8 hours and recorded. The GMR and EMG signals were correlated with laparoscopically visible peristalsis. Intravenous hydration rate, urine output, intra-abdominal pneumoperitoneum pressure, and anesthetic concentration were also documented during the observation period. The rate and frequency of peristaltic waves were recorded. No attempt was made to study the amplitude of the action potentials, as it depended on the distance between the electrodes and the ureteral musculature firing units. The signals from the magnetic sensor were correlated with the proximal and distal EMG signals to confirm that the signal picked up by the sensor was indeed a propagative peristaltic wave. We performed the above evaluation in four pigs without stents to evaluate the magnetic sensor's ability to detect ureteral motility and its consistency.

After confirming that the sensor was sensitive and accurate in identifying the mechanical movement of peristaltic wave, a randomized comparison of the acute effects of ureteral stents was performed along with the control ureter. Eighteen pigs were

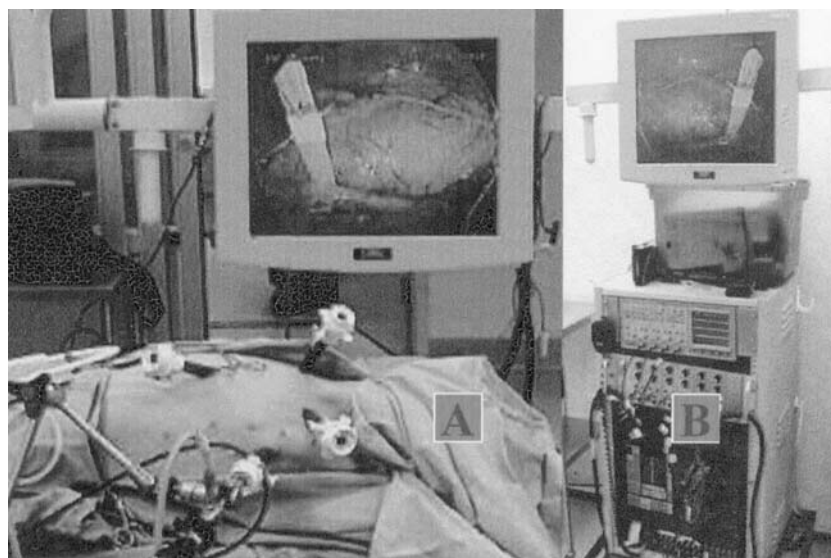


FIG. 3. Experiment set-up with trocar placement (A) and oscilloscope displaying electromechanical signals (B).

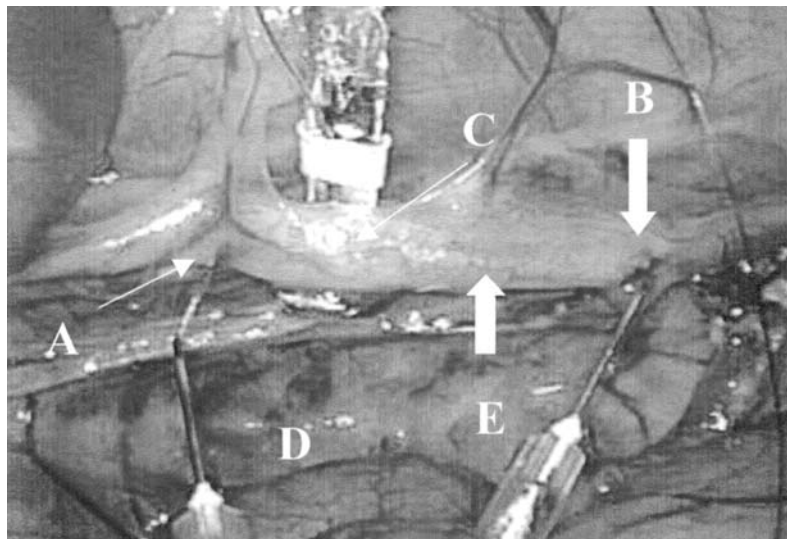


FIG. 4. Laparoscopic view of deployed proximal and distal EMG wires (A, B), GMR sensor (D), and neodymium magnet (C) on ureter (E).

used in the study: six control animals, six with 4.8F stents—three silicone-based (Percuflex Hydroplus™, Microvasive®, Watertown, MA) and three polyurethane-based (Mardis stent with Hydroplus coating™, Microvasive)—and six with 7F stents, three silicone based and three polyurethane based. Assignment to the various groups was random. All experiments were performed unilaterally without disturbing the contralateral side. The ureteral peristalsis was monitored for 8 hours in each animal, after which the EMG electrodes and the sensor were removed, and the animal was allowed to recover from anesthesia. After 1 week, ureteral peristalsis was reevaluated for 4 hours, the animal was sacrificed, and the kidney and ureter were retrieved for histologic examination.

For animals assigned to receive stents, after deployment of the EMG electrodes and the magnetic sensor, the ureter was observed for peristaltic activity for 30 minutes. The animals were then repositioned, and, after retrograde urography to confirm normal anatomy, a double-pigtail stent was placed over a guidewire in the study ureter under fluoroscopic guidance. The stented ureter was monitored continuously for 8 hours, with data recording for 15 minutes of each hour. The ureteral activity was reevaluated after 7 days.

Fisher's exact non-parametric test was applied using the SAS system to compare the different conditions tested for each stent.

RESULTS

Preoperative urine culture showed no infection in any of the animals, and the serum creatinine was normal preoperatively and at the 1-week postoperative follow-up. Implanting the EMG electrodes, magnet, and GMR sensor took an average of 30 minutes (range 20–48 minutes). An average basic peristaltic rate of 2/min (range 1–6/min) was observed. Also, the peristaltic waves occurred at irregular intervals; the frequency distribution was not constant. The intervals between waves ranged from 3 to 45 seconds. Peristalsis occurred in waves with activity for 3 to 8

minutes and then no activity for another 2 to 6 minutes. The waves propagated mostly in an antegrade fashion. However, occasionally, spontaneous retrograde peristalsis, which was incomplete, was observed.

A consistent correlation was found between laparoscopically observed peristalsis and the peristalsis detected by the EMG electrodes and the magnetic sensor. The EMG action potentials were characterized by multiphasic bipolar spike potentials with rapid onset and return to the baseline (Fig. 5A). The signals from the magnetic sensor were characterized as unipolar smooth deflection and bell shaped (Fig. 5A). The EMG activity preceded the mechanical activity recorded by the magnetic sensor by a few milliseconds. The propagative peristaltic wave seen visually correlated with the proximal EMG, magnetic sensor, and distal EMG signals on the oscilloscope. The peristaltic wavelength and propagative speed differed from one pig to another. The velocity of the waves was 2 to 6 cm/sec in the unstented ureter. Ventilatory and bowel movement artifacts were shown on magnetic sensor recordings as small low-amplitude deflections. Diuresis with rapid intravenous fluid infusion and furosemide produced a distended ureter appearing full throughout its length. Rarely, weak peristalsis (1/min) was observed, culminating in an aperistaltic state with no EMG or magnetic sensor activity 25 to 30 minutes after the onset of diuresis.

There was no change in the endoscopically visible baseline peristalsis before and after deployment of the EMG electrodes and the magnetic sensor device, indicating that deployment of the devices themselves did not affect peristalsis. During the first 2 hours following stent placement, there was an increase in peristaltic activity (Table 1). The character of the EMG wave was similar to that seen without the ureteral stent except for the lower amplitude. The contractions were visible to the naked eye but appeared weak. During the next 6 hours, 4.8F-stented ureters showed return of peristalsis to the basal rate. One-week follow-up revealed no peristalsis in four ureters; two ureters manifested occasional fasciculatory movements without organized peristalsis. The 7F stent produced an increase in peristalsis similar

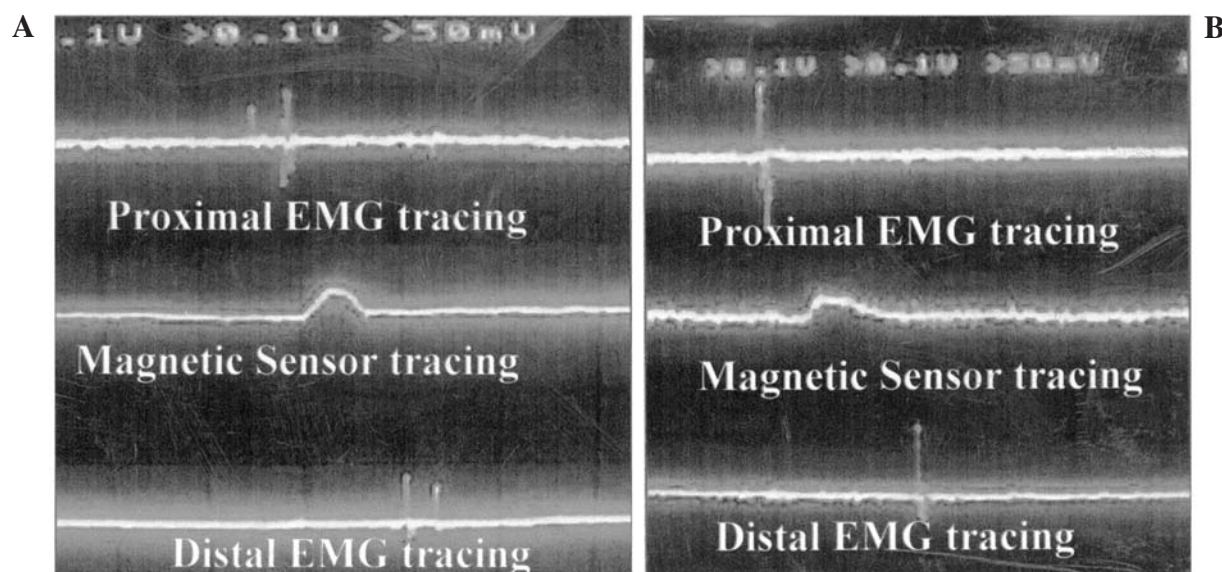


FIG. 5. EMG and magnetic sensor tracings in unstented ureter (A) and 2 hours after insertion of 4.8F stent (B).

to that seen with the 4.8F stents, but after 2 hours, gradual onset of decreased peristalsis leading to aperistalsis was observed in all ureters. During the gradual deterioration of organized peristalsis, incomplete disorganized fasciculatory electrical activity was recorded by the EMG electrodes. At 1 week, the 7F-stented ureters showed aperistalsis (Table 1). There was no significant difference in the peristaltic activity of ureters with silicone- or polyurethane-based stents. At 1 week, the stented ureters (both 4.8F and 7F) were grossly dilated, with marked inflammation. In contrast, at 1 week, the control ureters with no stents showed no dilation and no change in basal peristalsis.

DISCUSSION

Our study demonstrates a new method of studying ureteral peristalsis in a stented system using unique, laparoscopically deployable extraluminal sensors. The magnetic or GMR sensor is sensitive to small changes in the magnetic field and allows accurate measurement of displacements of an object in linear, radial, and rotational systems. This makes it applicable for measuring peristaltic activity in a tubular structure. The technology

is based on the giant magneto-resistive phenomenon, a recently discovered effect (1988) that is being used in the automobile and aircraft industries for various purposes (e.g., throttle positioning, wheel-speed sensing). To our knowledge, this is the initial application of GMR sensor technology in a macrobiological system.

Self-retained double-J ureteral stents have had widespread application in urologic practice for more than three decades. In 1967, Zimskin and colleagues³ reported on the first clinical use of self-retained stents for the treatment of ureteral obstruction. Over the ensuing 30 years, there have been several innovations in stent design in an effort to facilitate placement, improve flow, and decrease the associated symptoms. Stenting is regularly performed in humans, but to date, data on optimum stent size or configuration are sparse.⁹ Basic to such considerations is the determination of how stents function and their effect on ureteral smooth-muscle contraction. In the present study, we addressed the following questions: (1) how soon after placement does the stent impact the functional aspects of ureteral contraction with regard to peristalsis and electrical conduction? (2) how do changes in ureteral function differ with the size of the stent placed? and (3) does the composi-

TABLE 1. URETERAL PERISTALSIS (WAVES/MIN) WITH NO STENT OR WITH 4.8 F OR 7F URETERAL STENTS^a

Stent	Baseline	0–2 h	4–6 h	8 h	1 week
None	2 (1–4)	2 (1–3)	2 (1–6)	2 (1–4)	2 (1–4)
4.8F	2 (1–5)	4 (3–8)	3 (2–6)	2 (1–6)	0.013
	$P = 1.00$	$P = 0.04$	$P = 0.01$	$P = 0.81$	$P < 0.0001$
7F	2 (1–3)	4 (3–6)	0.018	0.01	0.005
	$P = 0.79$	$P = 0.06$	$P = 0.003$	$P = 0.007$	$P < 0.0001$

^a P values represent differences in stented v unstented ureters.

tion of the stent (silicone v polyurethane) affect the changes in ureteral peristalsis?

Dale and coworkers² demonstrated using microelectrodes inserted into the ureteral musculature that an intraluminal catheter connected to a pressure transducer (5F) indeed alters peristalsis. The regularity of peristalsis was increased by the presence of the catheter. In their experiment, there was no apparent obstructive pattern in the pressure recordings or increase in the urine flow rate to account for this alteration in peristaltic frequency. Thus, the presence of an intraluminal device such as a catheter or an indwelling double-pigtail stent appears to affect peristalsis. Therefore, to assess the effects of indwelling pigtail stents accurately, an extraluminal method of studying ureteral peristalsis would be necessary.

Ramsay and coworkers⁴ found that *in vivo*, most of the urinary flow from the renal pelvis to the bladder in a stented ureter occurs by bolus propagation around the stent. They also demonstrated that acute ureteral stenting causes a rise in the intrapelvic pressure, the magnitude of which depends on the size of the stent. Intrapelvic pressures return to normal values after 3 weeks of stenting, an effect the investigators attributed to mild ureteral dilation following stenting. Brewer and colleagues, in their *in vivo* study in a porcine model,¹⁰ evaluated the flow mechanics of several ureteral stents of different types and sizes, finding that total stent flow was dependent on both luminal and extraluminal flow. Luminal flow, but not extraluminal flow, rose with an increase in the internal diameter of the stent.

The increase in the rate of peristalsis immediately after the insertion of a stent, as seen in our study, may be related to the ureteral response to the luminal obstruction created by the stent. A strong association between increased frequency of ureteral peristalsis and ureteral obstruction has previously been reported.¹¹ Ryan and colleagues¹² reported on the acute and chronic effects of double-pigtail stents on upper urinary-tract motility and stone-transit time. They studied the ureteral pressure with an intraluminal 4F catheter and concluded that stents impair upper-urinary transit motility and may delay the passage of stones. However, the presence of the catheter in the ureter could itself have had an impact on peristalsis.

Our study demonstrated that a smaller stent (4.8F) yielded less impairment of peristaltic activity for the first 8 hours than the larger (7F) stent. Kinn and Andersen¹³ recently reported an *in vivo* porcine study on the impact of a stent on ureteral peristalsis. They used 4.2F pigtail stents bilaterally to analyze the frequency, velocity, and direction of the peristaltic waves using measuring electrodes twisted around a stent. They studied the effects of a 4.2F stent for 2 to 3 hours after its insertion and 6 weeks later, after its removal. There were no unstented control ureters or animals. Those investigators concluded that the presence of a stent impedes, weakens, and disrupts ureteral peristalsis at 6 weeks. Our findings are in agreement with their conclusions.

Our technique enabled us for the first time to evaluate the acute and chronic effects on ureteral peristalsis of two stent calibers and two stent compositions. In addition, using this extraluminal approach, we were able to compare these findings with peristalsis in unstented ureters. In our study, the smaller 4.8F stent had less impact on ureteral peristalsis; antegrade peristalsis continued, albeit to a diminished degree,

during the first 8 hours after stent insertion. In contrast, the 7F stent cause rapid disruption of peristalsis (within 3–4 hours), with an aperistaltic state developing during the initial 8 hours of observation. At 1 week after stent placement, both the small and the larger stents had induced an aperistaltic state. Study of normalization of ureteral motility after removal of an indwelling stent would provide additional information on stent effects on ureteral physiology.

CONCLUSIONS

The novel laparoscopic deployment of GMR technology with extraluminal ureteral application enables minimally invasive *in vivo* evaluation of both stented and unstented ureters. This experimental design affords the opportunity to evaluate the function of different stents and their effects on ureteral function. Our study suggests that a smaller-caliber stent has less acute effect on ureteral peristalsis than a larger stent. The particular stent composition does not seem to make any difference, either acutely or at 1 week.

A better understanding of the ureteral physiologic response to stents and medications may yield improved endoscopic techniques and permit more expeditious evaluation of various stent prototypes. Magnetic sensor technology has the potential to enable study of the various effects of stents as well as pharmacological agents on ureteral activity. It also has potential to facilitate the study of peristaltic activity in all other biological tubular structures, ranging from larger ones such as the bowel to even the most diminutive such as the vas deferens and the fallopian tubes. A new technology is upon us; the fruits of its application beckon.

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