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ORIGINAL PAPER

A.-C. Kinn · H. Lykkeskov-Andersen

Impact on ureteral peristalsis in a stented ureter. An experimental study in the pig

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Abstract Peristalsis was examined in ten pigs with stented ureters. In five of the animals, the stents were inserted 6–8 weeks before examination, which was performed using a 3.5 Ch catheter equipped with thin copper wires in two sites 10 cm apart. This set-up enabled an analysis of the frequency, direction and velocity of the peristaltic waves to be made. When diuresis was gradually raised, the frequency and velocity of the contractions usually increased in normal ureters, whereas we observed a decline in both of these parameters. There was a statistically significant difference in the lower frequency in the long-term stented animals. Retrograde peristalsis, aberrant waves and incomplete contractions were common in the ureters after prolonged stenting, and urine flow was greater around than through the stent. Our results suggest that the flow of urine is obstructed by a ureteral stent, and they support clinical data showing that such devices prolong the time it takes for a stone to pass to the bladder.

Keywords Ureteral peristalsis · Ureteral stents · Stone disease

Introduction

The purpose of double J ureteral stents is to ensure good drainage of urine from the kidney to the bladder in patients with obstruction. The urine flows both through and around the stent, and there is a continuous interchange between these two paths via the numerous side holes in the stent. Stents are normally used on a temporary basis, for instance while waiting for the spontaneous migration of ureteral stones. However, long-term use is common in patients with conditions such as pelvic tumours, inflammatory strictures or retroperitoneal fibrosis.

There are few examinations reported regarding the impact on urine flow and ureteral peristalsis by indwelling stents. Ramsay and co-workers [12] studied the effects of stents on ureteral peristalsis and urine flow in pigs and observed changes in the amplitude and frequency of peristaltic contractions, which they interpreted as signs of persistant obstruction. However, these investigators did not determine whether the indicated changes were due to the presence of the stent or also persisted after its removal.

It is assumed that the transport of urine from the kidney to the bladder is primarily myogenic and that it is triggered by the gradual stretching of smooth muscle fibres in the caliceal walls. The urine is propelled towards the pyeloureteral junction but also spreads centrifugally to all parts of the pelvis. The contractions continue down along the ureter, and, when complete, they counteract backflow by coapting the ureteral wall. The urine is driven in front of a contraction and immediately fills the ureter down to the ostium with a short delay at the crossing of the iliacal vessels, which seem to cause a certain resistance [9]. In general, the velocity of a contraction is 2–5 cm/s [3] although the speed of the urine is much faster at the front of the bolus and varies with the tonus of the muscular wall, the width of the ureter and the resistance of surrounding tissues [1].

Increased diuresis is normally followed by a transient rise in the peristaltic frequency and, in general, the volume of each bolus increases. When urine production is very high, the ureters dilate, and the boluses grow larger and finally coalesce; the contractions become incomplete and have smaller amplitudes and lastly the ureter functions as an open funnel [7, 18].

During ureteral obstruction, there is an initial rise in the intrapelvic pressure, contraction frequency increases and the amplitude of each wave in the ureter is higher.

A.-C. Kinn (✉) · H. Lykkeskov-Andersen
Department of Experimental Clinical Research,
Skejby Hospital, Aarhus University, Denmark
E-mail: annecharlotte@kinn.se

A.-C. Kinn
Department of Urology, Karolinska Hospital,
171 76 Stockholm, Sweden

With a longstanding obstruction, the ureter widens above the obstacle, and the amplitude of the contractions decreases. The timing of the contractions is disturbed and the propagation of the waves is retarded over the obstructed area and, in some cases, the waves gradually disappear. In addition, there are often retrograde contractions from new foci, acting as pacemaker sites, as well as incomplete or superficial waves. After 6 weeks of obstruction there is often a complete lack of coordination between the pelvic and ureteral peristalsis [6].

Our study was focused on the changes in peristaltic activity that are induced by an indwelling stent.

Methods and materials

Ten female landrace pigs, 4–5 months old and weighing 32–36 kg, were used in the experiments. Five of them had stents that were introduced into the left ureter at the start of the study; the other five had indwelling stents that had been cystoscopically inserted under anaesthesia 6–8 weeks before examination. The pigs were sedated with ketamine i.m. (25 mg/kg body weight), then anaesthetized with pentobarbital via an ear vein, and subsequently intubated and ventilated with oxygen-nitrogen and 1.5% halothane.

The femoral artery and vein on the left back limb were dissected free for measuring arterial blood pressure and for taking venous blood samples. Thereafter, an extraperitoneal vertical midline incision was made, and the bladder was opened. If a stent had been inserted 6–8 weeks previously on the left side, it was removed, and urine samples were collected from the ureter for bacterial cultivation. Ureteral catheters (4 Ch) were pushed up over guidewires to both renal pelves. With the guidewires palpable in a calyx, the catheters were passed through the parenchyma. Infant feeding tubes (5 Ch) with multiple side holes were then sutured to the catheters and pulled into the renal pelves as nephrostomies, these tubes were securely sutured to the renal capsule. The ureteral catheters were thereafter exchanged to 4.2 Ch double-J stents.

On the *right side* the ureter was cut just above the ureteral orifice. In three of the pigs two test tubes were anchored in such way that the urine oozing from the ureter itself could be collected separately from the urine passing through the holes in the curved end of the stent. In the other seven animals all urine was collected in a single test tube.

On the *left side* the double J stent introduced into the ureter was constructed with eight ring electrodes made of very thin laquer coated copper wire. The copper wires were twisted around the stent in sets of four. Two electrodes at each location were used for excitation, and the other two for detecting changes in the cross sectional area of the ureter; the upper and lower set were 10 cm apart. The stent easily passed up the ureter over a guidewire; the ureter of a 4–5 months-old pig is about the same size as that of an adult human. The excitation electrodes were connected to a generator in an impedance planimeter (GateHouse, Denmark) producing a constant alternating current of 250 μA at 5 kHz. The detection electrodes were connected to an impedance measuring unit in the impedance planimeter.

The difference in voltage between the inner detectional electrodes was considered to represent the cross-sectional area of the ureter. The sodium ions determine the electrical conductivity and for a given current the potential difference is given by Ohm's law : V = IZ = Id(delta CSA)-1, where I is the current introduced and V the potential voltage difference, Z is the electrical impedance of the urine in the cylindrical ureter, delta the conductivity of the urine, d the distance between the detection electrode and CSA is the cross sectional area. I and d are constants, and, if the conductivity of the urine is also constant, V should be inversely proportional to CSA. However, in our experiments, there was a large variation in diuresis and thus in sodium content and osmolality . Therefore it was only possible to measure the diameter of the urine bolus during stable diuresis but not to compare the ureteral sectional area on different occasions, as was intended. Not withstanding, the special catheter did make it easy to ascertain whether contractions were incomplete or if there was retrograde peristalsis.

The pigs received an intravenous infusion of saline (300 ml/h) and the urine output from the right kidney was continuously collected and measured during 15-min periods. In three pigs, the urine passing through and around the stent was collected separately. On the left side, data on ureteral peristalsis was registered for later analysis of the frequency and velocity of the contractions. The basal period continued for up to 2 h, or until the diuresis was stable. After 1 h of steady, low urine production, diuresis was enhanced by i.v. supply of 20 mg Furosemide, and the same three parameters were measured. Lastly the pelvic catheter was used for the infusion of saline (5 ml/min) and changes in the same parameters were again recorded.

At the end of the experiments, the pigs were killed by an intravenous injection of potassium chloride and the ureters were cut opened and examined to determine the location of the catheters and stents and possible anatomic anomalies.

Analysis

The mean diuresis from one kidney was calculated per minute. Values of 0.5–1.0 ml/min were considered to be low and those >2 ml/min to be high. Contraction frequency and velocity were calculated during periods of low and high diuresis and during infusion of 5 ml/min via the nephrostomy. The frequency of the contractions during 15 min periods was determined in the recorded curve and the mean value at each level of diuresis was determined. The contraction velocity was calculated based on the amount of time that lapsed between the start of contractions at the proximal and distal pair of electrodes and the mean values were determined for 15 min periods.

The signals were amplified, A/D converted, stored, reciprocated and later analysed on a PC by means of software specially developed for this purpose (Supermingo version 2.1 and MotAn version 3.3, GateHouse, Denmark). Before initiating an experiment, the catheter was calibrated in two plastic cylinders (respective diameters 7 and 10 mm) submerged in isotonic saline at 37°C.

Statistics

The data were analysed using repeated measures ANOVA, it was thus possible to compare the values recorded under different conditions in a single pig. ASAS software with a compound symmetry model and probability 0.95 were used to determine significance.

Results

In the pigs in which urine flowing through and around a stent was collected separately, the volume passing around the device was 3–4 times higher (Fig. 1). With increasing diuresis the amount delivered via the side holes to the ureteral orifice increased more than the urine volume passing in the stent (Fig. 1). The intrapelvic pressure increased from 3.5 cm H20 in low diuresis, to 8.1 cm H_2O during high diuresis and reached 15.2 cm H_2O during saline infusion.

Changes in peristaltic rate

The five animals that received a ureteral stent at the onset of the experiments (group A), exhibited regular

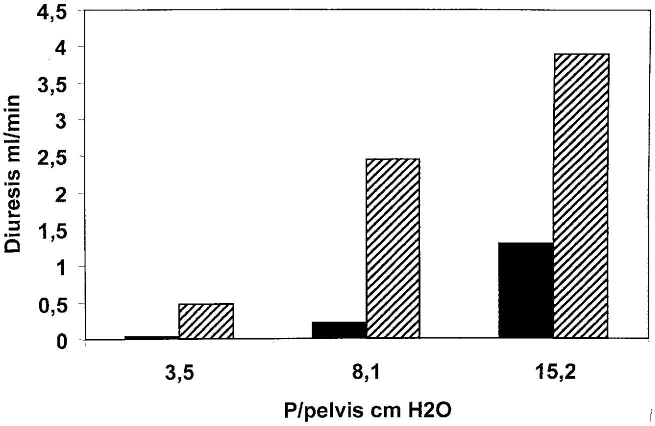


Fig. 1. Urine transport through the holes in the curved bladder end of the ureteral stent (*black bars*) and direct via the orifice (*striped bars*) in different grades of diuresis and renal pelvic pressures

peristalsis with a mean contraction frequency of 4.0 waves/min (range 2.8–4.9) during low diuresis (0.5–1.0 ml/min) in both the proximal and in the distal part of the ureter (Fig. 2). With increased diuresis (> 2 ml/min) the frequency decreased to 2.5 waves/min (range 0.8–4.0) (Fig. 2). During very high fluid transport (> 5 ml/min) there was a clear reduction in the registered contractions, and, in three of the pigs, it was difficult to follow the direction of the peristaltic waves, because they were very small and gradually disappeared altogether.

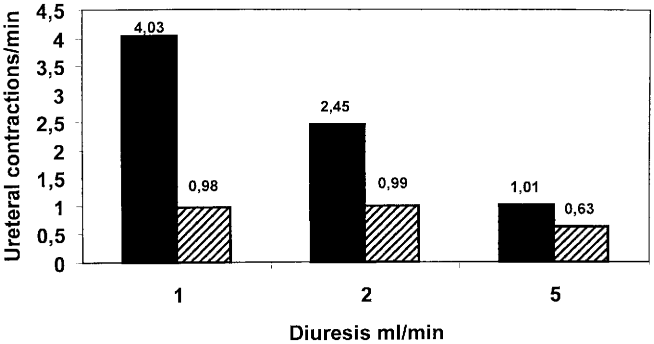


Fig. 2. Contraction frequency in stented ureters at different grades of ureteral flow. *Black bars* denote pigs in group A with stents introduced at the start of the experiment, while *striped bars* denote pigs which had also had an indwelling stent for 6–8 weeks before the actual study. At low diuresis (0.5–1 ml/min) and high diuresis (2–3 ml/min) there is a significantly lower frequency ($P = 0.007$ and 0.047, respectively) in long-term stented ureters than in directly stented ureters. There is no significant difference between the groups during saline infusion of 5 ml/min in the renal pelves

In the five pigs that received indwelling stents 6–8 weeks before starting the experiments (group B) we observed a mean of one contraction (range 0.5–1.9) per minute during low urine flow, which is significantly lower than the corresponding value for group A ($P = 0.0007$; Fig. 2). When diuresis reached 2 ml/min, the contraction frequency decreased, but the difference between groups A and B was smaller ($P = 0.052$). During saline infusion of 5 ml/min via the nephrostomy, all of the pigs displayed a low and irregular contraction frequency (Fig. 3), with no significant difference between the two groups.

Changes in peristaltic pattern

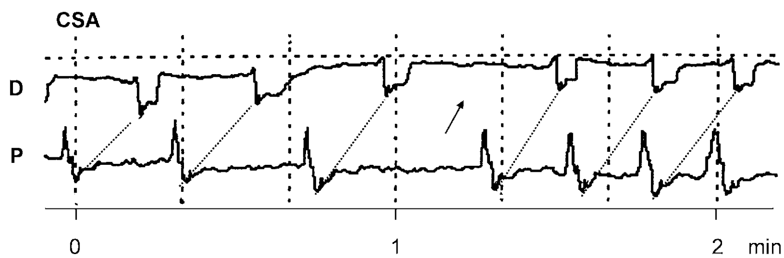
In the pigs with a stent placed in the ureter at the start of the examination, the peristaltic propagation was mostly regular and passed in an antegrade direction (Fig. 4) with a slower rate at high diuresis (Fig. 5). During low diuresis the contractions in the ureter passed primarily in the antegrade direction in both groups but in group B they were often incomplete and resulted in insufficient emptying of the urine bolus. At very high ureteral flow (5 ml/min or more) the contractions were, as a rule, incomplete and irregular in both animal groups (Fig. 3)

During all levels of diuresis, retrograde contractions originating from ectopic foci in the distal part of the ureter were often observed in group B, but rarely in group A (Fig. 6). At times, the disruption of peristalsis in group B was so extensive that it was difficult to monitor the propagation of waves. During some periods, even bladder activity was propagated in a retrograde path along the ureter. In three of the pigs, there was no co-ordination at all between the waves in the proximal and distal parts of the ureter. (Fig. 7). During the very high fluid transport induced by infusion, the contractions were extinguished in four of the pigs.

Changes in peristaltic velocity

The contraction velocity was analysed in the curves recorded on a longer time scale by ascertaining the time elapsed between the contractions at the first and the second sets of electrodes (Fig. 8). During low urine transport, the contraction velocity varied from 0.8 to

Fig. 3. At very high ureteral flow (5 ml/min or more) the contractions are incomplete and irregular. (Pig II, group A). Abbreviations as above



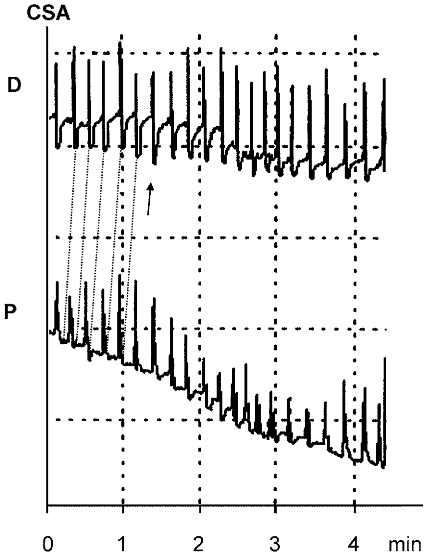


Fig. 4. Regular propagation of four ureteral contractions per minute with a mean contraction velocity of 1.2 cm/sec. Urine flow is low (1.2 ml/min). Abbreviations: *P* and *D*, the proximal and distal part of the ureter; *CSA*, the cross sectional area of the ureter. The distance between the two scale lines on the y axis signifies an increase in CSA of 20 mm^2 during the build up of a urine bolus. The calibration was performed in elastic cylinders of known caliber, but the given values are not exact, because the sodium content of the urine varied with different grades of diuresis. Corresponding peristaltic events are marked and the peristaltic direction shown by *arrows*. (Pig II, group A)

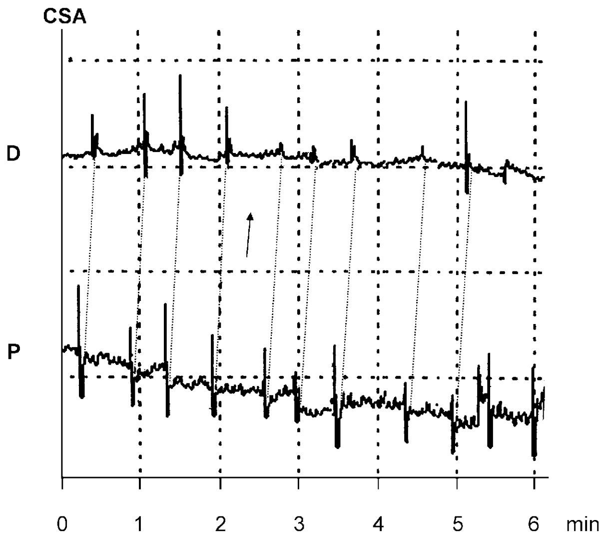


Fig. 5. At high diuresis the frequency is lower and the propagation is still regular but slower. The amplitudes are wider meaning a larger volume in every urine bolus. Abbreviations and symbols as in Fig. 4. (Pig II group A)

2.3 cm/s in group A (mean 1.0 cm/s) and from 0.7 to 1.8 cm/s (mean 0.8 cm/s) in group B, with no significant difference between the groups. During intensive diuresis, the contraction velocity was reduced to 0.48 cm/s in group A and to 0.39 cm/s in group B. During pelvic infusion of 5 ml/min the contraction velocity was 0.70 cm/s in group A and 0.53 cm/sec in group B. However, in group B, retrograde contractions were so common or the amplitudes so small that it was often difficult to achieve reliable determinations of the velocity.

At the time the animals were killed, the ureters that had had an indwelling stent were wider, but, when they were cut open, no calcifications or strictures were observed, nor were there any signs of infection.

Discussion

The use of ureteral stents has increased due to technical advances providing more pliable and durable manufacturing materials. Better guide wires and pushers have also been introduced, which facilitate the correct placement of the devices. Although stents essentially ensure a safe flow of urine from the renal pelvis to the bladder in patients with calculi, they do entail certain disdvantages such as infections and calcifications [5]. In addition, some patients experience flank pain, probably caused by vesicorenal reflux or dysuria due to bladder irritation by the curved tail of the stent [11, 13] . These side effects should not be overlooked when considering the introduction of a stent.

Furthermore, for quite some time it has been a matter of debate whether the passage of a stone is actually facilitated by a widened, relaxed ureter combined with reduced pressure in the upper urinary tract or if a strong ureteral peristalsis is more effective in this context [4, 15]. In a randomized clinical study, Bierkens and coworkers [2] found that stone migration in patients was prolonged by the presence of a ureteral stent, which agrees with the finding of experiments on animals which had artificial stones placed in the proximal part of the ureter [15].

In accordance with a report by Payne and Ramsay [10] we found that stents provoked considerably reduced peristalsis in pigs, which implies that these devices may also prevent ureteral passage of a calculus in humans. This conclusion seems sound, considering the clear similarity between porcine and human kidneys in regard to macroscopic and microscopic architecture, distribution of neuroreceptors, intraureteral pressure and electrophysiological conditions.

Our results show that both ureteral motility and amplitude and the directions of the peristaltic waves are altered. Also, in the above reports on animal experiments, peristalsis in the presence of a ureteral stent had a reduced frequency and the amplitudes of the peristaltic waves became smaller [8, 15]. The decreased peristaltic frequency also remained low in dogs after the removal of the stents [8], and although the contractility gradually recovered, there was still a lower frequency and lower contraction amplitudes after 12 weeks. In previous studies these findings were considered to be signs of persistant obstruction which was further indicated by the discovery of muscular hypertrophy and collagen deposition in the muscular wall of the ureter [15].

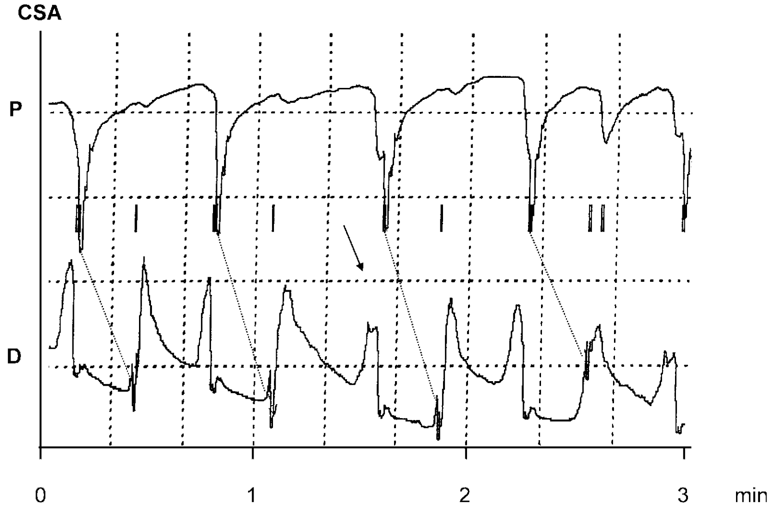


Fig. 6. In pigs which had had a long-term stented ureter the contractions often already start from ectopic foci in the distal part of the ureter at low diuresis (1.5 ml/min, pig VII, group B). Abbreviations as above

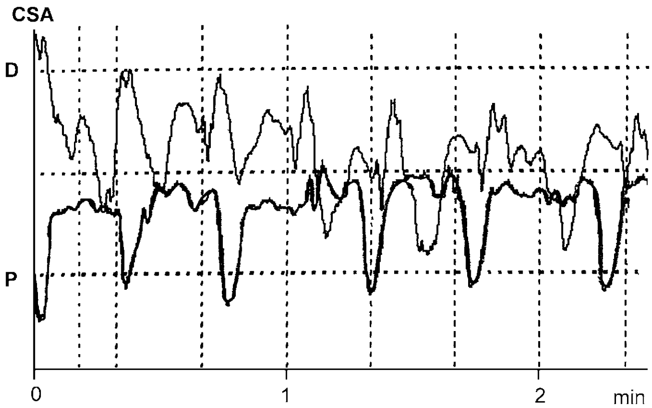


Fig. 7. With increased urinary flow the peristalsis is totally irregular and there is no cooperation between the proximal and distal part of the ureter in pigs which had had indwelling stents (Pig VIII, group B). Abbrevaitions as before

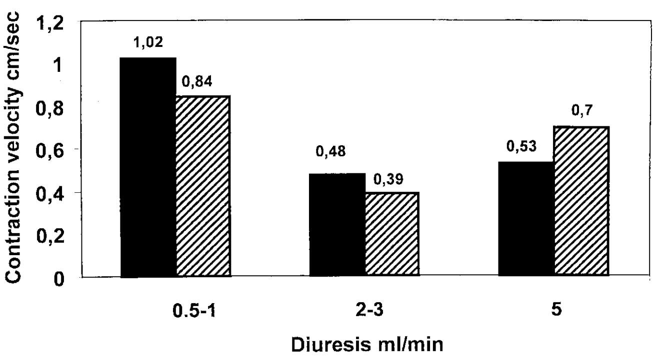


Fig. 8. Contraction velocity in stented ureters at different grades of diuresis and with an infusion of 5 ml/min in the renal pelvis. *Black bars* refer to pigs in group A (recently stented ureters) and *striped bars* in group B (long-term indwelling stents). There are no significant differences between the groups

However, the common consequences of obstruction are increased peristalsis and higher amplitudes [17] which do not correspond with our findings of decreased frequency and lower amplitudes in all stented ureters, but specially in the widened ureters in the pigs which had earlier had an indwelling long-term stent. It may be that the combination of dilatation and the presence of a foreign body in the ureter, as compared to a persistent obstruction, has a greater effect on the contractility of the smooth musculature in the ureter and therefore leads to incomplete contractions. Muscular spasm and oedema evoked by the stent my also contribute. The telescopic dynamic retraction of the distal portion of the ureter within its sheath may also be extinguished by the stent and have an influence on peristalsis.

The velocity of the contraction waves did not differ between the pigs that were long- and short-term stented, and it was not markedly affected by increased diuresis.

Nevertheless, the most notable finding in our study was that ureteral peristalsis was substantially disturbed in the pigs with long-term stenting. This is indicated by the common occurrence of retroperistalsis, and occasionally also propagated detrusor contractions, as well as the irregular and often disrupted ureteral activity, even during low diuresis. The disordered peristalsis with incomplete contractions was probably caused by dilatation of the ureter, which may have reduced the force of the contractions in the muscle walls and presumably led to ineffective urine transport. According to Vereecken [17] ectopic or antiperistaltic activity is always caused by a factor evoking a local depolarization of the muscle cells as, for example, obstruction with ureteral distension, damaged ureteral tissue but also the mere presence of an intraluminal catheter. Retrograde contractions also often occur when a kidney is drained by a nephrostomy, but in our study they frequently appeared even though the nephrostomy was closed and used for pelvic manometry.

In as much as we used measuring electrodes that were twisted around a stent, it was impossible to include unstented control animals. Moreover, we only studied peristalsis for up to 7 h after the long-term stents were removed from the pigs, and it is conceivable that normalization of the ureteral motility would have occurred with time, even if other investigators have shown longstanding changes [15]. Further studies with longer follow-up are necessary to clarify this matter. Experiments using stents with different calibres would also provide valuable information.

We chose a 4.2 Ch catheter in our study. With this rather small lumen, only about 25% of the urine passed through the holes of the curved tail: instead the main portion of the urine passed around the catheter. It is thus likely that a calculus would become lodged in this device. Previous studies have shown that urine drainage around a stent increases over time as the ureter gradually widens [14, 16].

Our results indicate that the presence of a stent impedes, weakens and finally disrupts ureteral peristalsis. If the purpose of stenting is to achieve a good and long lasting urine transport, as is necessary in patients with malignancies or inoperable strictures, it is probably best to choose a stent that is as wide as can be tolerated. In patients with ureteral stones thin stents can temporary lower the raised intrapelvic pressure but still permit effective ureteral contractility and should therefore be preferred. Stents should presumably be removed as soon as clinically possible to enhance stone migration.

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