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Ureteric Function and Upper Urinary Tract Urodynamics in Patients with Stones in Kidney and Ureter

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1. Introduction

The clinical manifestations of stone disease, its complications and prognosis are closely bound up with the upper urinary tract (UUT) urodynamics. In urological clinical practice, obstruction and peculiarities of pelvicalical anatomy are usually taken into consideration as the major urodynamic factors in discussions of stone disease pathogenesis (Husmann et al., 1995; Matin & Strem, 2000; Grampsas et al., 2000; Sorensen & Chandhoke, 2002). Less attention is given to the role of functional UUT abnormalities especially in ureteric peristalsis because of designing a method to record human ureteric activity without causing interference is difficult (Shafik, 1996; 1998; Kinn, 1996; Davenport et al., 2007; 2011).

From the viewpoint of UUT physiology, it is known that smooth muscle contractions are essential for urine transport from kidney to the urinary bladder. This process is performed by two major mechanisms: the passive flow driven by hydrostatic pressure, and active one resulted from contractile activity of the smooth muscles in the wall of urinary tract. Both mechanisms are well studied in vivo and in vitro on various animal models under physiological and pathological conditions, and now they are discussed in relation to human urological diseases.

The coordinated muscular contractions propagating along the ureter and providing the active mechanism of urine transport have been generally termed as 'ureteral peristalsis'. Contractions of smooth muscles within UUT are evoked by action potential activity in atypical smooth muscle cells termed interstitial cells of Cajal (ICC)-like cells or pacemaker cells (Hannappel & Golenhofen, 1974; Lang & Klemm, 2005; Pezzone, et al., 2003; McHale et al., 2006; Hashitani et al., 2009; Lee et al., 2011). The role of the ICC-like system in the urinary tract is discussed in relation to variety of severe congenital and/or acquired urological diseases, such as hydroureter and megaloureter (McHale et al., 2006). Whether these atypical pacemaker activities within ureter can disorganize UUT peristalsis has not been elucidated for the stone disease. However, it was demonstrated that excitation of latent pacemakers by noxious/irritant stimuli occurring during a passage of a stone or a bacterial infection can generate the antiperistaltic contractile waves producing urine reflux toward the kidney (Santicioli & Maggi, 1998). Moreover, in a divided ureter, the normal antegrade electrical activity can be replaced by retrograde contractions occurring in different UUT

parts independently (Tindall, 1972). Cellular and molecular processes directing normal ureter development as well as disease mechanisms leading to obstructive uropathies are still unknown (Airik, et al., 2010). Coordinating proximal-to-distal peristalsis of the upper urinary tract is commonly defective in congenital diseases (Hurtado, et al., 2010). However, in clinical trials, functional disturbances in UUT are little examined, and there are only limited data on the role of ureteral peristalsis in the course of stone disease (Davenport et al., 2006, 2011).

Under the resting conditions, regular UUT electrical and contractile function is characteristic of normal peristaltic urine transport. The action potentials spreading to the membrane of ureteral smooth muscle cells induce their contractions employing the mechanisms common for other smooth muscles. The rhythmic contractions of ureter are driven by propagating membrane depolarization. Myogenic and neurogenic nature of muscle contraction is still discussed on the basis of calcium and Rho-kinase cellular contractility mechanisms and peculiarities of UUT innervation (Kobayashi 1965; Notley, 1971; Santicioli & Maggi, 1998; Levent & Buyukafsar, 2004; Weiss et al., 2006; Hurtado, et al., 2010; Grisk, et al., 2010).

Enhancement in urine production results in stretching the ureter and increasing the volume of urinary bolus. The increasing urinary flow is accompanied with growing rate of peristaltic contractions till the ureter takes the shape of an open duct (Constantinou, 1974; Constantinou & Yamaguchi, 1981; Harada et al., 1984; Kim et al., 2002). In such cases, urine passage is passive, which does not use peristaltic movement of ureteric wall, so urine is driven entirely by hydrostatic pressure gradient from the areas of high pressure to those of low pressure.

The role of intraluminal pressure in the UUT was thoroughly discussed for experimental physiological and pathological conditions, as well as for clinical settings (Davis, 1954). It was shown that pressure developed by peristaltic wave is responsible for the unidirectional transport of urinary bolus being therefore a kind of "active" antireflux mechanism. Contractile function of proximal and distal ureteral segments and the influence of baseline ureteral distending pressure upon ureteral luminal pressure generation are discussed with respect to ureteral function during urinary outflow obstruction (Rasidovic et al., 2010). Moreover, there are data indicating peristaltic pressure as a vital requirement for the complex process of urine secretion, conduction, storage, and expulsion from the body. Peristaltic contractions of the pelvic wall were proved to be an effective mechanism that concentrates urine in the renal papilla (Dwyer & Schmidt-Nielsen, 2003). At present, the pressure measurements have been used to study medication effects on ureteral peristalsis (Davenport et al., 2006; Pick et al., 2011) or they are fulfilled in order to protect kidney from harmful pressure increase during ureteroscopy (Jung et al., 2006; Page et al., 2011; Jung & Osther, 2011). Despite essential role of this urodynamic phenomenon for renal function, the dynamic changes in the renal pelvis pressure during stone disease course were little studied.

The above shortly described physiological mechanisms of ureter functioning can be helpful to explain the urodynamic disorders in patients with stone disease. Objective information on ureteral function status in each patient, the knowledge on urodynamic transporting mechanism, whether it happens by passive hydrodynamic flow or by active peristalsis, can be useful to prognosticate and avoid the possible complications such as urine stagnation and refluxes.

2. Methods of the UUT urodynamic functional diagnostics

In clinical practice, visualization methods are commonly used to assess urodynamic disorders. They are based on ultrasound, X-ray, isotopic, and magnetic resonance examinations yielding information on UUT size and structure, and on stone or stricture location (Kinn, 1996). The qualitative data on ureteral function given by visualization techniques is UUT dilation, and an indication on peristaltic frequency (Kim et al., 2008).

In experimental studies, more functional parameters are harvested by physiological methods, but these possibilities are seldom used in clinical setting. The physiological measurements include electromyography, as well as impedance and intraluminal pressure measurements along a ureter.

Electromyographic studies have established the characteristics of ureteric excitation (Shafik, 1996; Roshani et al., 2000). The impedance measurements are based on field gradient principle for quantification of cross sectional area of ureteral urine bolus (Harada et al., 1984), or as a function of ureteric motor activity (Roshani et al., 1999 2000; Kinn, & Lykkeskov-Andersen, 2002).

Electromyography together with impedance method based on cross sectional area of urine bolus measurement was reported to be carried out in laboratory and clinical experiments (Harada et al., 1984). The authors used the probe consisted of ureteral catheter with 4 ring impedance electrodes and a bipolar ring ureteromyographic electrode. As urine bolus passed through the impedance electrodes, the value of impedance represented the cross sectional area of the urine bolus.

As a function of ureteric motor activity, the impedance measured between thin copper electrodes placed on a catheter in two sites 10 cm apart enabled to analyze frequency, direction, and velocity of peristaltic waves (Kinn, & Lykkeskov-Andersen, 2002). With a single catheter recording EMG, impedance, and the pressure changes, the characteristics of mechanical activity during ureteral peristalsis, propagation velocity of the peristaltic wave through ureter, and urine bolus transport were quantified (Roshani et al., 1999).

For simultaneous study of electrical and mechanical parameters of ureteral peristalsis in pigs, electrical potentials from ureter were lead with bipolar steel-wire electromyography electrodes delivered laparoscopically, and the mechanical movements were monitored by giant magneto resistive sensors mounted on custom-made aluminium strips (Venkatesh et al., 2005; Page et al., 2011).

Peristaltic frequency, conduction velocity, and intraureteral pressure was assessed in an animal model and in six patients who had undergone ureteroscopy with the commercial ureteral pressure transducer catheter (Young et al., 2007). It was demonstrated that instrumented human ureter displayed a variable response related to previous physical or pharmacologic effects.

Ureteric peristalsis characterized with contraction frequency, pressure and velocity measurements was recorded in eighteen patients with the help of ureteric pressure transducer catheter (Davenport et al., 2007). The authors concluded that despite various limitations intrinsic to ureteric catheters, these measurements provide some useful information when used to record the response to an intervention in the same patient.

In our experimental study we simultaneously recorded electromyogram, electromagnetically measured urine flow rate, intraluminal pressure, and impedance via special probes consecutively applied to the same ureter in dog (Fig.1). This record illustrates physiological events in the ureter obtained by direct measurements. The electromyogram spikes precede the peaks of flow wave that initiates pressure rise and corresponds well in time to impedance oscillations. The ureteric impedance decreases maximally during the passage of the urine bolus associated with maximal increase in the flow volume curve.

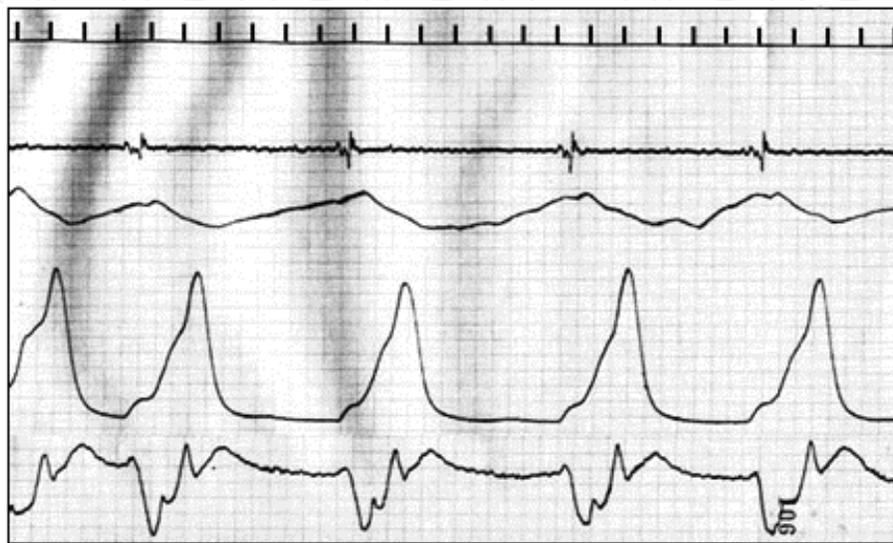


Fig. 1. An example of simultaneous ureteric peristalsis registration in a healthy anesthetized dog. Channels (top-down): time controller (1 sec); electroureterogram (mV); urine flow rate (ml/min); pressure (cm H₂O); impedance ureterogram (Ohm)

Thus, the routine recording of ureteric excitation can be supplemented with the data on mechanical activity during ureteral peristalsis assessed with impedance and pressure measurements. Anyway, very little data are available on ureteral peristalsis in the clinical settings, which actualizes functional diagnostic of urodynamic conditions in patients with stones in UUT.

In our further work, multichannel ureter impedance recordings were used to study ureteral function under normal and pathological conditions in dog experiments, and also in clinical examinations of urological patients with stone disease, hydro- and ureterohydronephrosis (Mudraya et al., 2001; 2007; 2011).

The multichannel impedance ureterography (MIUG) method is carried out using a 8F probe inserted into a ureter of a patient endoscopically. The measuring probe is equipped with 9 consecutively incorporated separate electrodes. The current (2 mA and 32 kHz frequency) is driven to extreme (the 1st and the 9th) electrodes of the probe while the interim electrodes served for impedance measurements. The potential differences from the consecutive pairs of measuring electrodes (2-3; 3-4; 4-5; 5-6; 6-7; 7-8) permit to obtain the impedance waveform of the adjacent parts of the ureter during its activity. The impedance converter "RPKA2-01" ("Medass", Russia) and special software (MCDP32) provides simultaneous 6-channel monitoring of the instantaneous impedances within consecutive ureter segments.

The assessment of the function of a ureter is fulfilled automatically and processed according to the following parameters at impedance ureterogram as Fig. 2 shows. The peristalsis amplitude (A) is the maximal deflection of impedance during urine bolus passage and contraction of ureter. The ureteral wall tone (T) is an inverse value of impedance deflection taking place immediately to rhythmic breath activity. The peristalsis rate (f) is calculated from time period between consecutive contractions. The duration of a contractile wave (D) is a distance between the start and the end point of ureteral contraction corresponding to impedance curve deflection from isoelectric line. Calculation of conduction velocity was made using a single contraction recorded by six electrode pairs on the probe - the velocity of contractile wave (or urine bolus propagation V) is the product of division of the constant distance between the first and the last pair of potential electrodes (75 mm) and the time needed for propagation of the wave along this distance. In addition to quantitative parameters of ureteric function, the multichannel impedance monitoring made it possible to evaluate the qualitative characteristics of UUT peristalsis. These parameters include the shape and direction of the peristaltic wave propelling (antegrade, retrograde, cystoid, chaotic), and their rhythmicity. The normal (antegrade) peristaltic wave usually appears in the upper regions and spreads down the ureter (Fig.3, a). The retrograde (reflux) contractile wave propagates in the opposite direction that can be reliably monitored (c). Cystoid contractions recorded with MIUG represent simultaneous contractions in ureteral region 7.5 cm in length (ureteral cystoid located across the probe), which is equal to the distance between the 1st and the last 6th pair of registering electrodes on the probe (b, d).

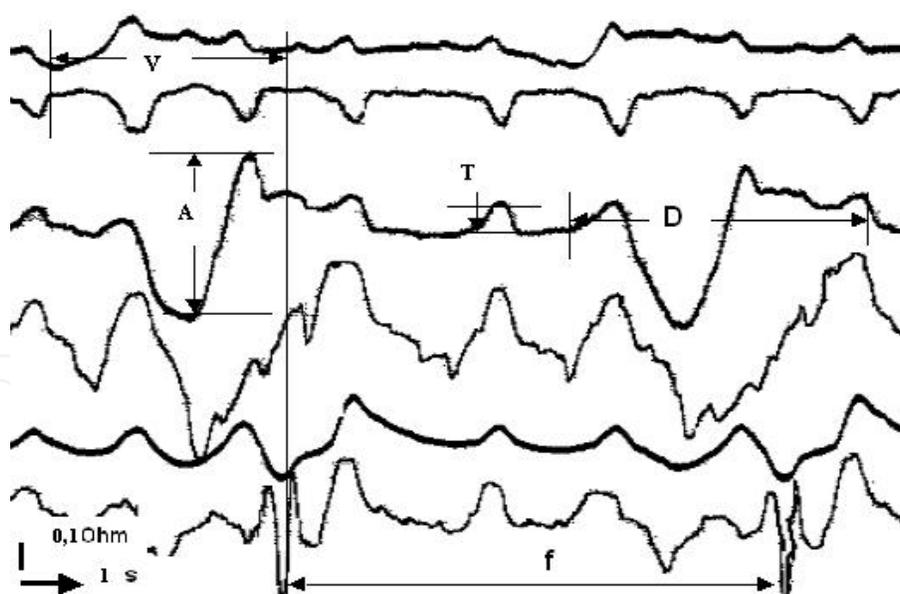


Fig. 2. Example of MIUG with ureteral peristalsis parameters. A- peristalsis amplitude; T- ureteral wall tone; D- duration of a contractile wave; f- time period between consecutive contractions; V- velocity of contractile wave

Here our experience is described on MIUG and intrapelvic pressure measurements performed within the routine of complex urodynamic examination of the patients with stone disease. On the whole, 250 patients with various urolithiasis clinical histories were

randomly involved and examined in different patients groups composed according to duration and severity of stone obstruction, inflammatory complications, and some treatment procedures. The status of UUT urodynamics was assessed with standard ultrasonic and X-ray examinations. MIUG method has been employed in patients during diagnostic ureteroscopy (URS), lithotripsy procedures and ureteral stent exchanging. Electromanometric pressure measurements were fulfilled in patients who had clinical indication to nephrostomy. The renal pelvic pressure (RPP) measurements have been performed via nephrostomy tube in the course of obstructive stone disease management and inflammatory complication medical or operative treatment.

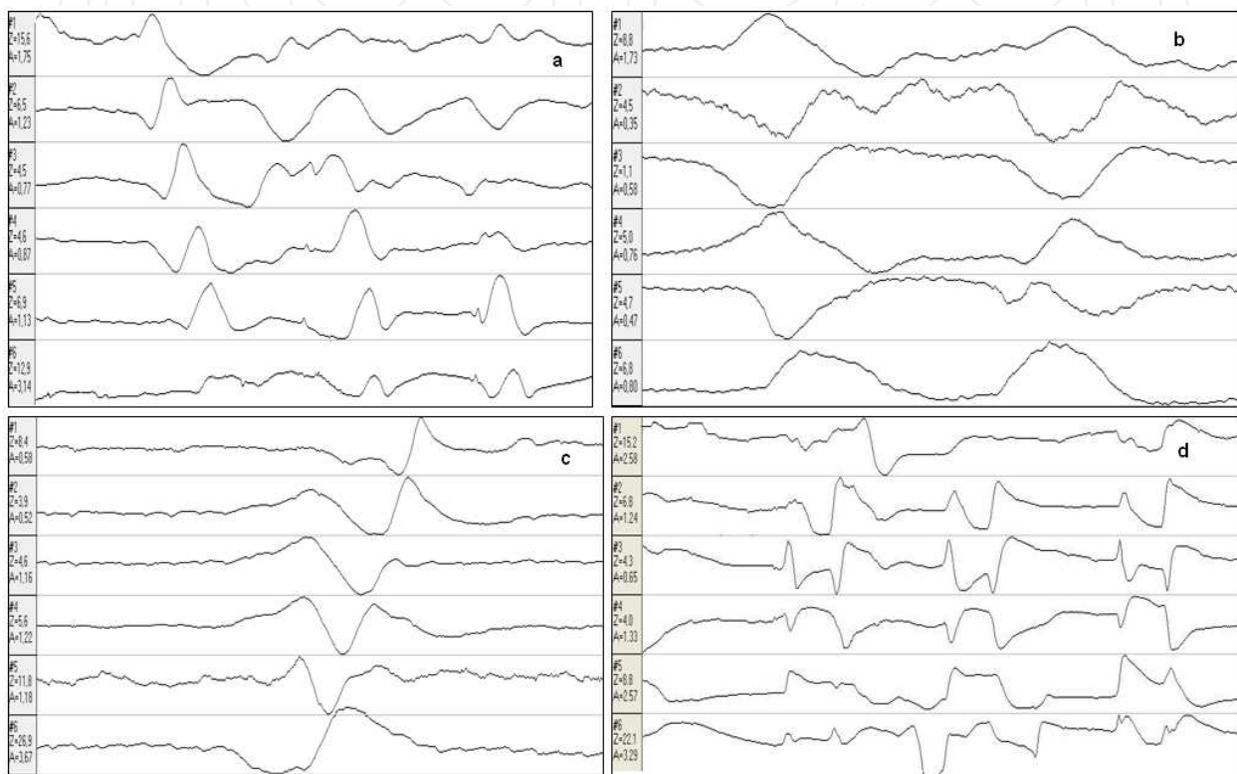


Fig. 3. Examples of ureteral peristalsis obtained by MIUG in patients with stone disease. a- antegrade contractile waves; b- cystoid contractions; c- retrograde (reflux) peristaltic wave; d- deformed multitoothed cystoid contractile waves; each record time is 20 sec

3. Characteristics of ureteral function in patients with stone disease.

Abnormalities in ureteral peristalsis were common in all patients with urolithiasis although their severity differed individually. Ureters showed variable patterns of peristalsis immediately after probe insertion, which were probably related to previous physiological and pathological conditions.

On the whole, the patients with stones in UUT were characterized with decreased amplitude of ureteric peristalsis, increased ureteral wall tone, and larger peristalsis rate as compared to the normal ureters (Table 1). The data were obtained in 43 patients with UUT stones before lithotripsy session (of them 7 patients with solitary kidney) and 3 patients with normal ureters during diagnostic URS.

Parameters	Ureteral segment		
	proximal	middle	distal
Patients with both kidneys			
Peristalsis amplitude (Ohm)	0.70±0.08	0.61±0.15	0.61±0.13
Ureteral wall tone (Ohm ⁻¹)	5.5±0.9	4.5±1.4	5.8±1.3
Peristalsis frequency (min ⁻¹)	3.2±0.8	3.1±0.6	3.8±0.9
Solitary-kidney patients			
Peristalsis amplitude (Ohm)	1.12±0.25	1.18±0.26	1.11±0.23
Ureteral wall tone (Ohm ⁻¹)	4.2±0.5	2.5±0.4	4.7±2.5
Peristalsis frequency (min ⁻¹)	4.6±1.4	6.5±1.4	4.4±1.8
Patients without stone in the UUT			
Peristalsis amplitude (Ohm)			2.1±0.9
Ureteral wall tone (Ohm ⁻¹)			2.2±1.4
Peristalsis frequency (min ⁻¹)			2.0±0.7

Table 1. Parameters of ureteral peristalsis in patients with stones in UUT and patients with normal ureters

Three patients with normal ureters were subjected to diagnostic URS for roentgen-negative stones. Of them, two patients had unilateral UUT stones, and one patient had a benign prostate hyperplasia. No stones or urodynamic disorders were revealed in the examined ureters of these patients. All of them demonstrated the examples of rhythmic antegrade peristalsis in distal ureteral cystoid. In the normal ureter, urine is propelled antegradely towards the bladder, while the contractions spread downstream along the ureter.

Among the patients with stone disease, there were those whose ureters demonstrated pronounced activity with differently directed contractile waves in the ureter (Fig.4, a). In addition, there were patients with aberrant chaotic peristalsis (Fig. 4, b). These parameters were characteristic of each patient's ureteral peristalsis and in average did not significantly differ in the upper, middle, or distal cystoid of the ureter. In the patients who had solitary kidney, the ureteral function differed from that in the patients with both kidneys. In the case of solitary kidney, enhanced peristalsis amplitude and higher rate of contractile activity attest to hyperfunction of the ureter (Table 1).

According to the mean values of peristalsis amplitude and ureteral wall tone, 33 patients with stone disease were divided into four groups (Table 2). It is supposed the high amplitude rhythmic contractions and the low wall tone are characteristic of the normal ureteral function (Table 2, group I). Such peristalsis was observed only in 23% patients examined with MIUG, whose ureters looked like the normal ones. However, the most often characteristic of the ureteral function in examined patients with stones in UUT was combination of the low amplitude of contractions with enhanced ureteral wall tone indicating severe dysfunction in ureteric peristalsis (Table 2, group IV). Such peculiarities in ureter performance were observed in 42% patients. These quantitative characteristics are corroborated by observations on the increasing number of the patients with peristaltic arrhythmia, contractile wave deformity (e.g. the appearance of the multitoothed contractions) and peristaltic disturbances manifested by retrograde and cystoid waves.

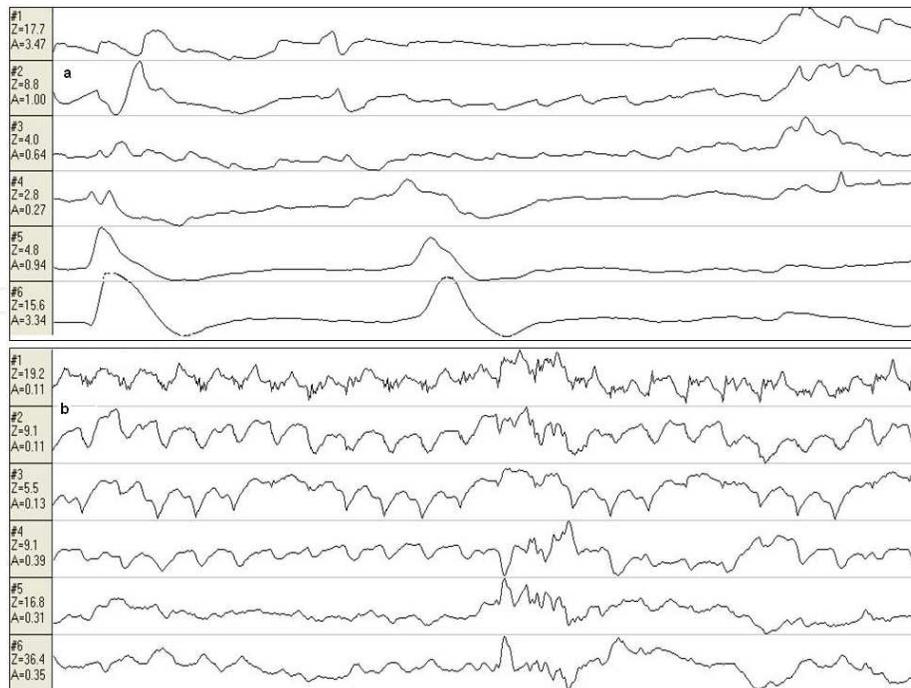


Fig. 4. Examples of ureteral peristalsis obtained by MIUG in patients with a- strong contractile activity in the ureter, and b,- with aberrant peristalsis; each record time is 20 sec

Patient groups	I	II	III	IV
Peristalsis amplitude (Ohm)	1.8±0.4	1.3±0.2	0.5±0.1	0.3±0.03
Ureteral wall tone (Ohm ⁻¹)	2.2±0.1	7.9±1.8	2.9±0.2	13.2±2.1
Peristalsis frequency per minute	2.6±0.2	2.2±0.6	3.3±0.3	3.0±0.2
Qualitative peristalsis characteristics (manifestation percentage)				
Arrhythmia	52±6	30±5	86±8	84±7
Deformed contractions	51±3	50±3	71±6	84±5
Antegrade waves	100	68±4	19±3	34±5
Retrograde waves	50±4	50±5	73±6	87±7
Cystoid contractions	16±3	43±5	91±9	86±8

Table 2. Parameters of ureteral peristalsis in patients with stone disease according to MIUG data

Thus, the antegrade propagation of peristaltic waves along the ureter was characteristic of the normal ureteral peristalsis. It is reliable to show that in normal ureter, peristaltic wave travels from proximal to distal cystoid, i.e. antegradely. This antegrade peristalsis ensures urine transport from renal pelvis towards the bladder and serves to protect renal parenchyma, while the backflow of urine generated by retrograde contractile waves can induce back pressure and urine refluxes that are dangerous for kidney (Davis, 1954; Dwyer & Schmidt-Nielsen, 2003; Mudraya & Khodyreva, 2011). The cystoid contractions are supposed to represent simultaneous motion in ureteral cystoid that is likely referred to diuretic mode of urine transport through opened and dilated ureter. The deformed multitoothed contractions and peristalsis arrhythmia can be the features of ureteral wall irritation and repeated excitations of smooth muscle cells. These data corroborate the

opinion that irritation and stretch stimulation of the ureter by a stone may result in large uncoordinated peristalsis (Rose & Gillenwater, 1973; Davenport et al., 2006).

Among the examined patients, we couldn't find the differences in ureteral function depending on the patients' age and gender. However, the urolithiasis history was essential for appearance of ureteral function. The special features of peristalsis were observed in patients with renal colic, primordial, or permanent stones. They will be discussed further. In general, there was a tendency to smaller ureteral peristalsis amplitude (0.51 ± 0.16 Ohm) and higher (by 23%) ureteral wall tone in the patients suffering from stone disease for a long time, compared to the patients having stones for only short periods (1.16 ± 0.34 Ohm). The cystoid and retrograde contractions were prevailing among other kinds of peristaltic activity in the ureters of patients with long-term stone disease history, and the peristalsis rate was slower by 48% in them than in the patients who had stones for several months only (Fig. 5).

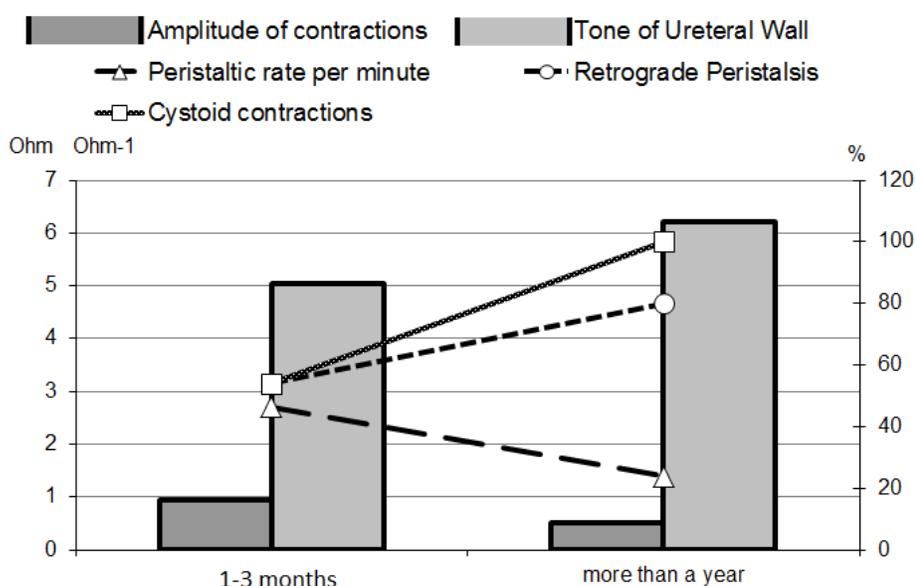


Fig. 5. General dynamics of ureter functional parameters in relation to duration of stone disease

4. Peculiarities of the ureteral function in patients with various stone position in UUT

Analysis of ureteral function has been performed for thirty patients with renal (8) and ureteral (22) stones in UUT. Of 8 patients with renal stones, 7 patients had unilateral and 1 had bilateral calculi. Of 22 patients with ureteral stones, 12 had urolith in the proximal ureter, while other had it in distal ureter (one patient had bilateral stones). In these patients, the diagnostic probe has been introduced into the distal ureteral cystoid, and peristalsis in the distal part of ureter was evaluated by MIUG.

Despite the fact that ureteral function parameters differed to a great extent among the patients, the peculiar features were observed in patients with various stone position in UUT (table 3). The average data show that patients with distal stones in UUT were characterized with decreased amplitude of ureteric peristalsis and increased ureteral wall tone compared to the patients with kidney and proximal ureteral stones. Thus, peristalsis was mostly

seriously disturbed and destroyed in the region of stone location. The weak irregular contractions were typical for the patients with distal ureteral stones (67%). Evident cystoid and retrograde contractions as well as poor chaotic peristalsis were typical for the patients with proximal ureteral stones. The peristalsis amplitude in these patients was higher than that in patients with distal stones but lower than that in patients with renal stones. Most patients with renal stones (82%) demonstrated active ureteral peristalsis: the contractile waves of antegrade as well as retrograde direction were observed along with ureteral cystoid contractions. The mean peristalsis amplitude was the highest in them compared to others, while the tone was the lowest than in patients with other stone location.

Parameters	Renal stones	Upper ureter stones	Distal ureter stones
Peristalsis amplitude (Ohm)	1.08±0.12	0.63±0.08	0.45±0.04
Duration of a contraction (s)	7.1±0.4	7.6±0.2	8.1±1.1
Peristalsis rate (min ⁻¹)	2.9±0.1	2.8±0.2	2.7±0.8
Tone of ureteral wall (Ohm ⁻¹)	4.2±0.5	4.8±0.3	7.2±0.9
Velocity of contraction (cm/s)	2.3±0.7	2.9	2.1
Qualitative characteristics of the peristalsis activity			
Antegrade waves (%)	56	17	22
Retrograde waves (%)	66	83	22
Cystoid contractions (%)	33	67	33
Aberrant peristalsis (%)	18	40	67

Table 3. Characteristics of distal ureteric peristalsis in patients with different stone location in UUT

The average data on the peristalsis rate and velocity of a contractile wave obtained with MIUG in normal patients and in those with kidney and ureteral stones ranged 2.0-2.9 min⁻¹ and 1.3-2.9 cm/s, correspondingly. Virtually the same data were reported for human ureter obtained by intraluminal ureteric pressure measurements: the peristalsis rate and conduction velocity respectively ranged 0-4.1 min⁻¹ and 1.5-2.6 cm/s (Davenport et al., 2007). Visualization technique yielded only the data for peristaltic rate 3.5 min⁻¹ in normal ureters, while the abnormal ureters were characterized with decreased or absent peristalsis (Kim et al., 2008).

Moreover, the results obtained with MIUG method showed that the following three parameters differed in the ureters with stones despite of their position from the ureters with no stones. The velocity of contraction tended to be greater by 64-125% in ureters with stone compared to the normal ureters (1.3±0.3 cm/s). In such ureters, the peristalsis rate was faster by 35-81% than the normal rate of 2.0±0.7 min⁻¹, while the contractile wave duration was shorter by 13-28% (compared to the normal value of 9.9±0.8 s). Such results may reflect the specificity of ureteral peristalsis in patients with uroliths in UUT. Probably, the stone-induced irritations trigger rapid and simultaneous (cystoid) contractions of the ureter. The pronounced organic changes in ureteral wall due to fibrotic processes are usually characterized by aberrant peristalsis in the region of stone location. In the case of proximal stones in UUT, the peristalsis disturbances and strong contractile activity in distal ureter can be explained by reflex irritation of ureteral wall with a stone. Diagrams 1-4 (Fig. 6) well

demonstrate differences in the parameters of ureteral peristalsis depending on stone position in UUT assessed by MIUG method.

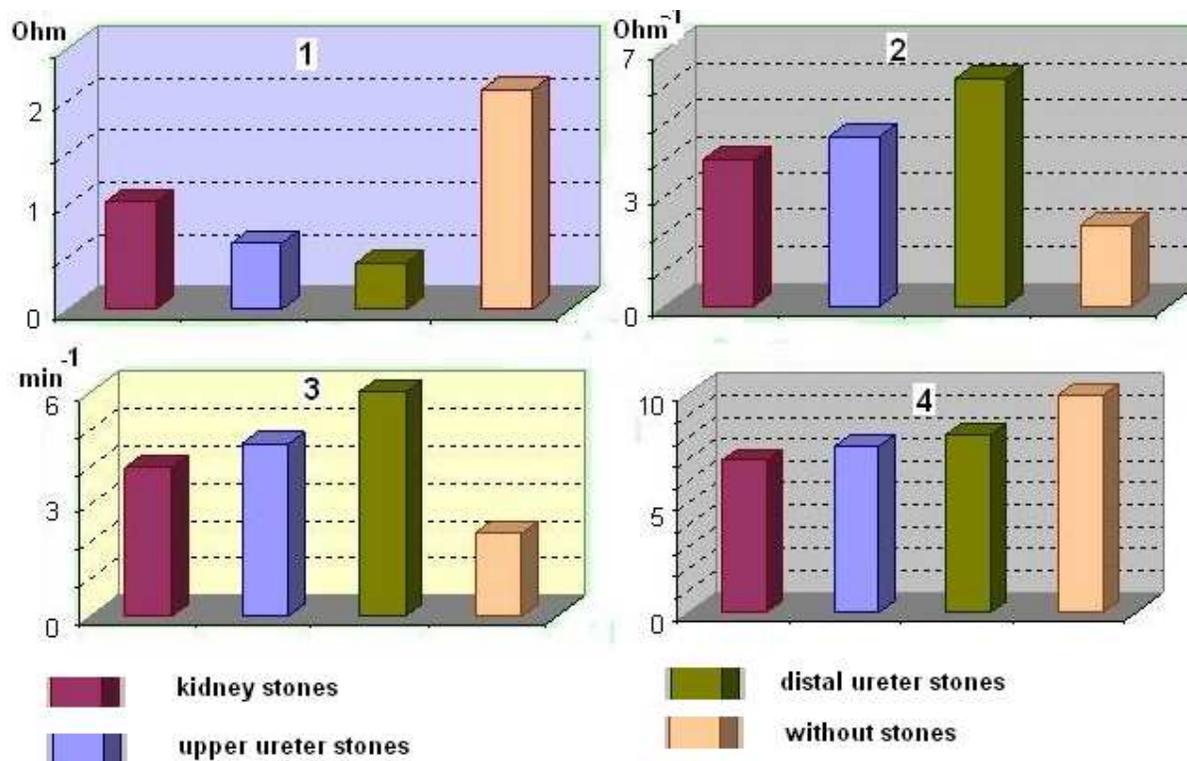


Fig. 6. Quantitative parameters of ureteric peristalsis in patients with various stone location compared to controls. 1- peristalsis amplitude; 2- ureteral wall tone; 3- peristalsis rate; 4- contractile wave duration

Thus, special features of ureteral peristalsis were observed in the patients with various stone position in UUT. Peristalsis amplitude was weaker, ureteral wall tone was higher, and contractile waves were faster and shorter in the ureters of patients with stones in the upper urinary tract as compared to the control group.

Figure 7 demonstrates that patients with the combination of differently directed contractile waves (antegrade, retrograde, cystoid) were numerous in a group with the renal stones. The antegrade contractile waves were observed in 50% patients with renal stones, and only in 9-12% patients with stones in ureter. The cystoid contractions were characteristic to all patients with uroliths in UUT (50-63%). The retrograde contractile waves in ureter were often observed in patients with the renal (67%) and proximal ureteral stones (54%), while the aberrant peristalsis was often recorded in patients with the ureteral stones (proximal - distal, 45-69%), in contrast to patients with the renal stones (10%).

The underlying mechanisms of urodynamic disorders seem to be different in patients with different stone position. Our data suggest that proximal UUT stones can disturb ureteral function producing vigorous uncoordinated contractions. On the contrary, the stones disposed in distal ureter which disturb its peristalsis can affect renal pelvic urodynamics, induce elevation in RPP, and/or dilation of the pelvicaliceal system.

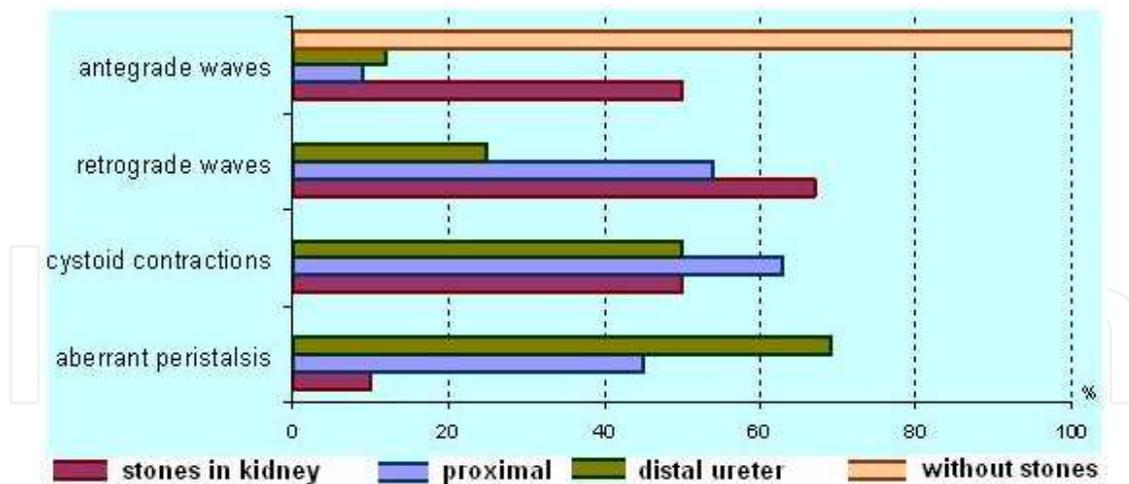


Fig. 7. Qualitative parameters of ureteric peristalsis in patients with various stone location compared to controls

5. Renal pelvis pressure dynamics in the course of stone disease

RPP have been measured in 73 patients with renal and ureteral stones, which had indications for urine diversion and underwent nephrostomy tube indwelling. An electromanometric transducer was hydraulically connected with the nephrostomy through a 3-way stopcock to enable urine outflow in the cases of pronounced pressure rise. The patients were randomized according to duration of stone obstruction, inflammation signs, the treatment history, and the level of obstruction.

Despite individual changes in the mean RPP in patients with UUT stones, analysis revealed different role of obstruction and inflammation in pressure elevation (Fig.8). The highest baseline pressure values in renal pelvis were recorded in the patients, who had stone obstruction accompanied with inflammation within up to 4-day period (25.0 ± 1.6 cm H₂O) and 5-10-day period (28.7 ± 2.6 cm H₂O). In the patients with ureters obstructed for 1-4 days that had no signs of inflammation, RPP was only moderately elevated (14.7 ± 2.9 cm H₂O).

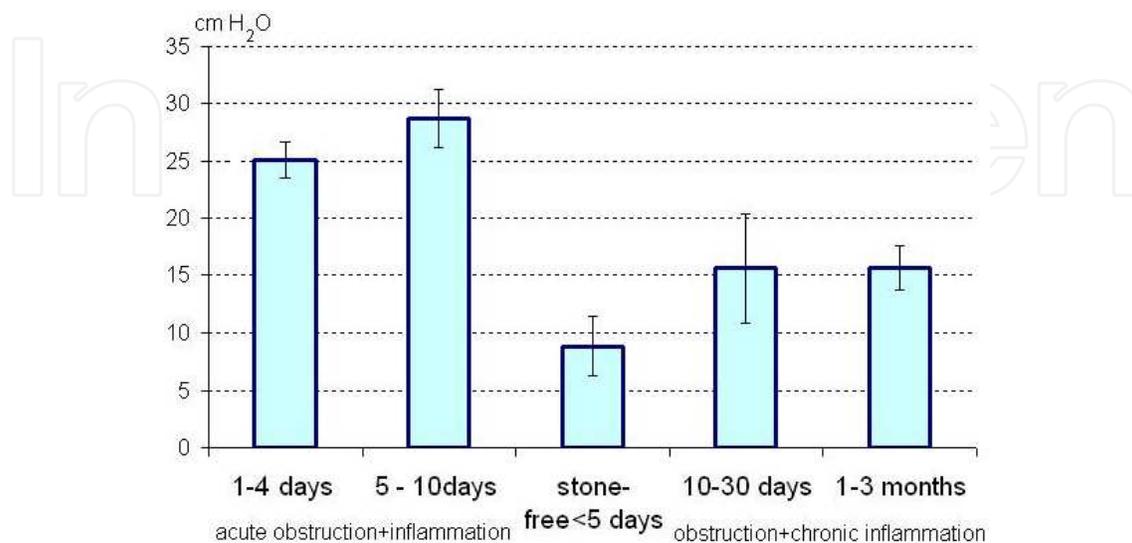


Fig. 8. Mean baseline RPP in stone disease patients in the course of treatment

In the unobstructed patients, in case of the short-term obstruction resolving, RPP quickly gave a reasonable fit to a normal sense (3.6 ± 1.4 cm H₂O). It is accepted that the normal baseline RPP values make up 10 cm H₂O measured in voluntaries (Shafic, 1998).

Thus, the results evidence that the main reasons of RPP rise in the patients with stones in UUT is obstruction and inflammation timing. The data on especially high RPP values registered on days 5-10 of acute inflammatory complication of obstruction, but not within the first 4 days, probably indicate significance of simultaneous rise in renal interstitial pressure and the development of inflammation progression, that is, the pressure in the intercellular spaces of the kidney (Davis, 1954). Smaller pressure variations produced by peristalsis or transmitted respiratory activity in renal pelvis during acute inflammation seems to corroborate this view. According to our results, the baseline RPP was higher (26.4 ± 1.5 cm H₂O) in the acute period of inflammation and obstruction (up to 10 day-period) than during chronic inflammation (15.6 ± 1.9 cm H₂O), while the mean delta pressure was much lesser in them (1.9 ± 0.2 vs 4.8 ± 0.3 cm H₂O), respectively. As this urodynamic parameter changes individually within a short or a long-term course of the stone disease, RPP can be considered as a reliable index of inflammation resolving and obstruction rescuing in patients, and therefore it can be used to predict future renal status.

The value of RPP depended on the level of obstruction being higher than 10 cm H₂O in the most of patients (90%) with distally located stones in UUT, and only in 59% patients with renal and proximal ureteral stones. In the 1-month period of obstruction and inflammation, the mean RPP was higher in the patients with distally obstructed ureters than in those patients that had ureters with proximally located concrements (21.8 ± 0.8 vs 12.4 ± 1.2 cm H₂O). However, during the later period of stone obstruction and chronic inflammation (1-3 months), RPP was quite similar in the case of distal as well as proximal stones (16.2 ± 0.7 vs 16.9 ± 0.8 cm H₂O).

RPP is an integral complex urodynamic parameter reflecting urine inflow (the quantity excreting by a kidney), elastic properties of the surrounding UUT wall, and the resistance to urine outflow depending on ureter capability and function. Eleven patients with partial obstruction and chronic inflammation who had nephrostomy were assessed by RPP measurements and following MIUG examination during URS. In them, special associations were noted between urodynamic disorders manifested by RPP elevation and ureteric peristalsis (Table. 4). Among patients with moderately increased RPP, 45% persons demonstrated weak ureteral contractions and pronounced ureteral wall tone. However, ureteric function was characterized by strong uncoordinated contractions and low ureteral wall tone in 36% patients.

RPP (cm H ₂ O)		Characteristics of Ureteral Contractile Activity			Ureteral wall tone (Ohm ⁻¹)
Baseline	Peristaltic	Amplitude (Ohm)	Duration (sec)	Frequency (min ⁻¹)	
14.0 ± 2.5	17.2 ± 2.4	1.04 ± 0.06	7.08 ± 0.28	3.2 ± 0.2	3.4 ± 0.2
16.4 ± 1.3	23.1 ± 3.4	0.29 ± 0.03	7.68 ± 0.61	3.1 ± 0.6	6.8 ± 0.7

Table 4. Characteristics of UUT urodynamics with respect to contractile function of distal ureter in patients with moderately elevated RPP

Thus, the mechanism underlying pressure elevation in renal pelvis varies with respect to ureteral function characterized by peristalsis amplitude and ureteral wall tone. Moreover, it seems to be different in the cases of renal and ureteral stone location. In the group with renal stones, RPP was pronouncedly elevated (>20 cm H₂O) in those patients that demonstrated persistent retrograde and cystoid waves, but it did not exceed 10 cm H₂O in the patients whose ureter demonstrated antegrade contractions. In the group with ureteral stones, an elevated RPP (>10 cm H₂O) was observed in the patients with weak chaotic peristalsis and enhanced ureteral wall tone. So, evident retrograde and cystoid peristaltic waves are supposed to provoke refluxes and urine stagnation contributing to pressure elevation similar to what takes place in patients with renal stones. Also, an aberrant peristalsis and increased ureteral wall tone correlated with elevated RPP and therefore induce urine stagnation as in the patients with ureteral stones.

Some important observations were made in the patients with residual stone fragments remaining in UUT for more than 1 month accompanied by chronic inflammation. Despite persistent adequate renal drainage per nephrostomy tube, RPP was moderately increased in these patients. Moreover, the patients that had lithotripsy procedures in anamnesis demonstrated even higher mean RPP (18.2 ± 1.3 , range 3.0 - 26.4 cm H₂O) compared to the patients with no previous lithotripsy procedures (15.6 ± 1.9 , range 2 - 18.8 cm H₂O). Moreover, the unobstructed patients without stones in UUT that have been examined before nephrostomy removal, demonstrated higher mean RPP if they had undergone operative treatment (18.9 ± 2.6 , range 9.0 - 24.0 cm H₂O) compared with the patients that had not been subjected to such treatment (13.3 ± 1.2 , range 9.0 - 20.0 cm H₂O). These results evidence that the operative treatment can affect RPP value.

Acute effects of lithotripsy procedures have been shown to manifest with rapid and short (several seconds) elevations in RPP up to 80 cm H₂O during some phases of the contact lithotripsy, and slow (several minutes) RPP elevations up to 34 cm H₂O were observed during ESWL sessions (Mudraya & Khodyreva 2011). We suppose those acute RPP elevations during lithotripsy sessions could be one of the mechanisms underlying moderate and stable renal pelvis hypertension. The importance to prevent chronically increased intrapelvic pressure is of concern (Davis, 1954). Nowadays, the procedures and medication to avoid sharp pressure rise during URS treatment are developing (Page et al., 2011; Jung & Osther 2011).

6. Efficacy of lithotripsy session in dependence on ureteral function and disorders in urodynamics

The results of extracorporeal shockwave lithotripsy (ESWL) procedure were evaluated in 36 patients according to stone-free rate, steinstrasse formation or residual stones in UUT with respect to stone disease history, and the ureteral functional parameters prior to this ESWL session.

As fig.9 shows, the best treatment results were achieved in the patients with colic demonstrating 60% stone-free rate, while the rate of residual stone formation was the highest in the patients who had stones in UUT for more than a month and ESWL sessions in anamnesis. Steinstrasse was often observed in patients who had surgery for stones (51%). The ureteral function in patients with short (1-4 days) period of stone disease was characterized with widely different contractile activity in ureteral parts before urgent ESWL.

The peristalsis amplitude was the highest (0.76 ± 0.26 Ohm) in the proximal ureter, while ureteral wall tone was especially elevated in the distal region of ureter (8.68 ± 1.41 Ohm⁻¹). Arrhythmic (67%), retrograde (80%), and cystoid contractions (100%) were dominant over the antegrade peristaltic waves in the upper, middle, and distal ureteral segments, respectively.

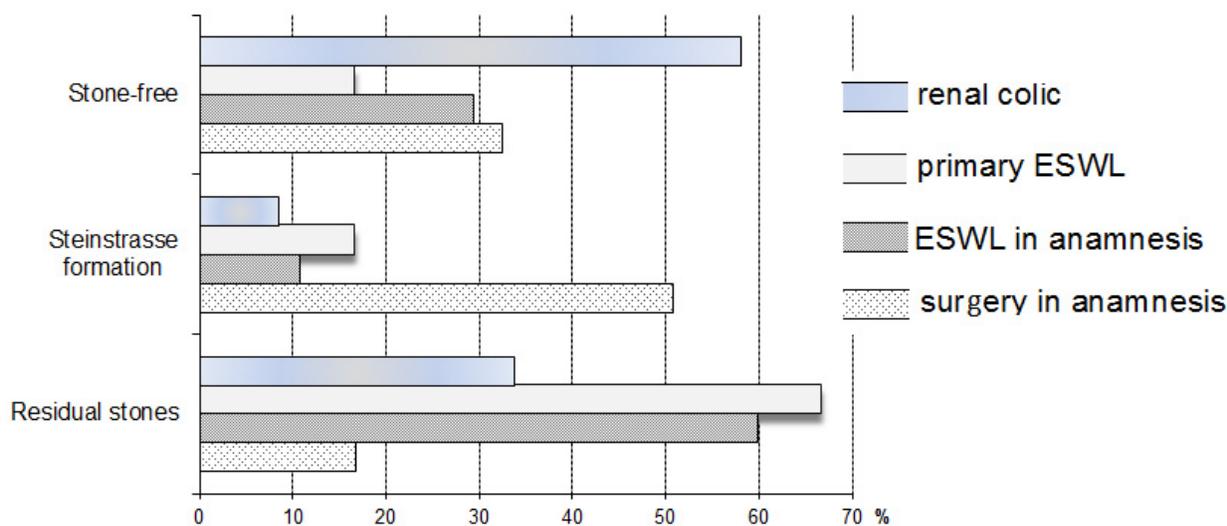


Fig. 9. Results of ESWL session with respect to stone disease history

Despite these peristalsis disorders, the most patients with colic episodes achieved successful stone removal after a single ESWL session. Long-term observation showed that these patients remained stone-free within 3-year follow up period. Only one (of seven) patient had inflammatory complications during the nearest postoperative period followed by nephrostomy. In this patient, high ureteral wall tone and vigorous retrograde contractions in the distal ureter were characteristic for ureteral peristalsis recorded by MIUG before ESWL session, and RPP recordings performed via nephrostomy tube showed rhythmic pressure elevations up to 30 cm H₂O evidently related to the retrograde ureteral contractions.

On the whole, the results evidence that the peristaltic derangement observed during the short-term period of urolithiasis might be reversible after emergent stone-obstruction removal. Thus, one can speculate that the patients with a short-term history of stone disease have safe ureteral smooth muscle wall function. In these patients, the peristalsis disorders observed prior to ESWL originate mainly from the reflex provoked by a stone not from organic changes in ureteral wall. Consequently, ability of ureter to propel urine properly can be quickly restored after restoration of its lumen patency.

The functional urodynamic disorders were pronouncedly aggravating during elongation of stones in UUT, and they changed individually in the course of treatment. Severe disorders in the ureteral peristalsis can be the complicating factor.

Taking into consideration the peculiarities of ureteral function (Fig.10), the high rate of steinstrasse formation can be explained by the weakest peristalsis amplitude and the highest

ureteral wall tone in patients with surgery in anamnesis, compared to other patient groups. On the contrary, the high rate of residual stone formation in the patients having stones in UUT for more than a month and subjected to ESWL can be explained by the strong peristalsis amplitude (69%) and frequent incidence of retrograde peristaltic waves (36%). In the patients without ESWL in anamnesis, the retrograde contractions were persistent only in 20% persons, while the rest 80% patients demonstrated weak peristaltic activity. Their peristalsis assumed cystoid (42%) character. In these patients, the high rate of residual stone formation was also observed.

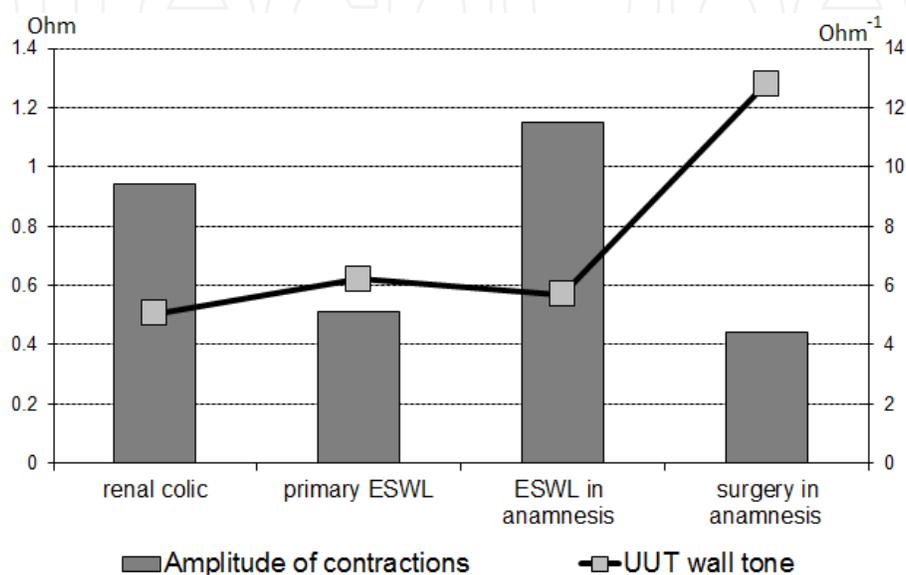


Fig. 10. Parameters of ureteral function obtained with MIUG immediately before ESWL session in patients with different stone disease history

The data on the greater ureteric peristalsis amplitude in patients with lithotripsy in anamnesis in comparison with the primary patients receiving only medication well agree with previously demonstrated higher values of RPP in the patient groups with nephrostomy. The primary patients who had no lithotripsy procedures in anamnesis were characterized with smaller mean RPP, and lesser peristalsis amplitude in ureters, as compared to the patients with ESWL in anamnesis.

Acute effect of another lithotripsy procedure on the parameters of ureteric function was evaluated in 12 patients who underwent contact lithotripsy (CLT). Of them, one patient was assessed by MIUG immediately during CLT session, 6 patients were examined by MIUG and RPP measurements before CLT, and 5 patients were examined after CLT (fig. 11).

In one patient examined immediately during CLT, peristalsis amplitude decreased by 45-50%, and the ureteral wall tone became 3-fold higher as compared to the baseline level. Similar changes were found in the groups of patients that were examined before or after CLT (Fig. 11): the peristalsis amplitude in distal ureter was smaller (0.50 vs 0.81 Ohm), the peristalsis rate was greater (3.3 vs 2.4 min⁻¹), and the tone was higher (6.8 vs 4.7 Ohm⁻¹) after this procedure. In addition, the patients subjected to CLT demonstrated moderately elevated RPP values (18.9±2.6 vs 15.6±1.9 cm H₂O) during the nearest postoperative period (3-7 days). The moderate but persistent RPP increments after endoscopic procedure are supposed to result from malfunction of the distal ureter. In the study using ureteral pressure

measurements (Young et al., 2007) it was noted that instrumented human ureter displayed a variable response that appeared to be related to previous physical or pharmacologic effects, and after ureteroscopy peristaltic recovery was variable.

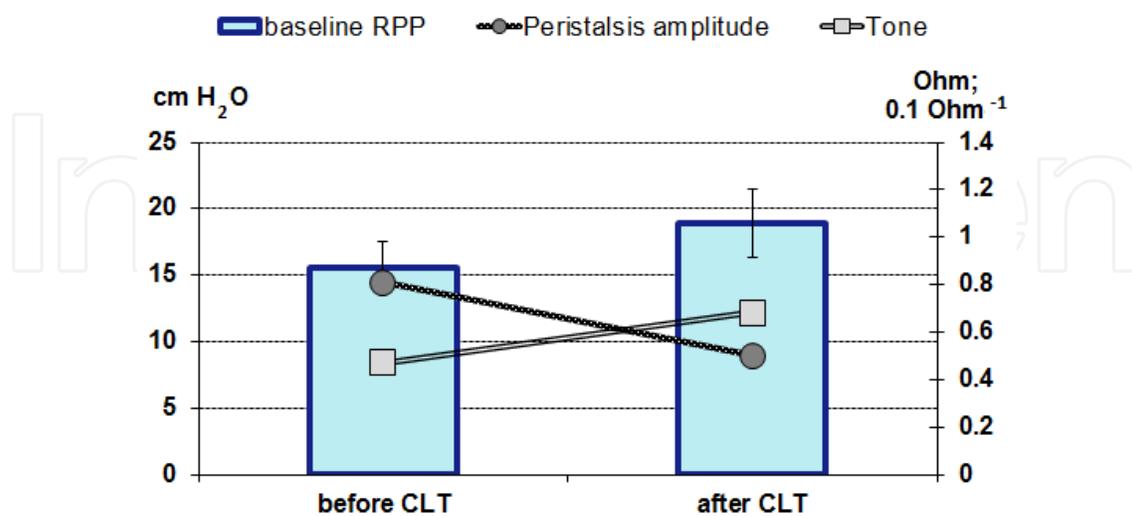


Fig. 11. Functional parameters of UUT urodynamics in patients underwent ureteroscopy (URS) and retrograde contact lithotripsy (CLT)

Thus, the reason of moderately elevated RPP in patients with history of stones for several months as regard to the ureteral function is supposed to concern in strong retrograde contractions, as well as weak contractile activity accompanied by high tone of ureter wall. Lithotripsy procedures are the factors aggravating the changes in RPP and function of ureter in the course of stone disease treatment.

Possible factor responsible for the results of stone elimination during ESWL session can be UUT dilation. The patients that have been subjected to ESWL followed by assessment of its efficacy were divided into three groups according to the range of UUT dilation that preceded this operative procedure (Fig. 12). Then, after lithotripsy session (7-10 day-period), the persistence or restriction of UUT dilation was analysed with respect to ureter functional parameters such as peristalsis amplitude and ureteral wall tone (Fig. 13) evaluated prior to this session.

Successful stone fragmentation and stone-free rate was achieved in 33% patients having no or moderate (<2 cm) UUT dilation, and only in 12% patients with >2 cm UUT dilation. In these patients, the ureteric function was characterized by pronounced retrograde and cystoid contractions (amplitude 1.09 ± 0.14 , and 1.11 ± 0.16 Ohm) and moderate or low ureteral wall tone (3.7 ± 0.52 , and 0.21 ± 0.01 Ohm⁻¹).

The residual stones after ESWL session were observed in 33% and 70% patients, respectively without UUT dilation, and with >2 cm UUT dilation. These patients' ureteral function was characterized by enhanced ureteral wall tone (9.61 ± 2.52 , and 3.10 ± 0.31 Ohm⁻¹) together with pronounced peristalsis amplitude (1.09 ± 0.19 , and 1.17 ± 0.09 Ohm). The steinstrasse was observed after ESWL session in 33% patients with no evident UUT dilation whose ureters demonstrated weak peristalsis activity (0.32 ± 0.12 Ohm) and high ureteral wall tone (5.18 ± 2.01 Ohm⁻¹), while the steinstrasse after ESWL session in the cases of dilated UUT, was formed in the patients (20%) whose ureters were characterized by strong ureteral contractions (1.97 ± 0.58 Ohm) and moderate ureteral wall tone (2.08 ± 0.51 Ohm⁻¹).

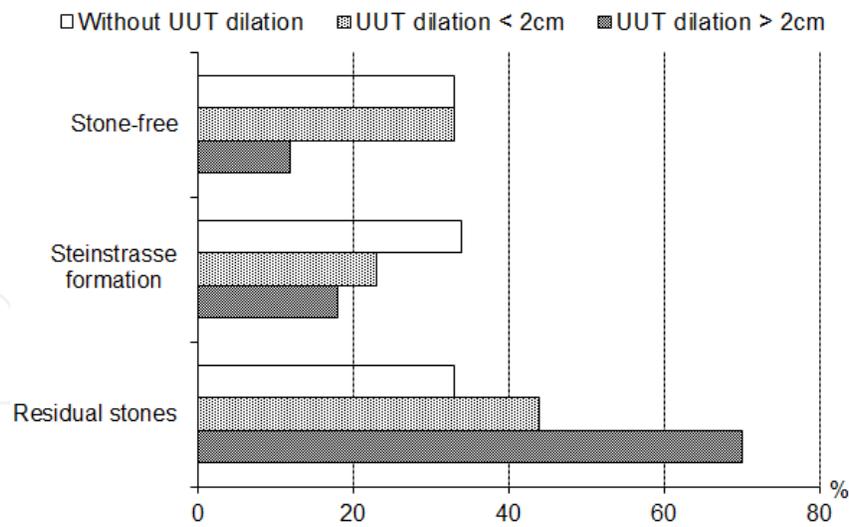


Fig. 12. ESWL session efficacy concerning the range of UUT dilation

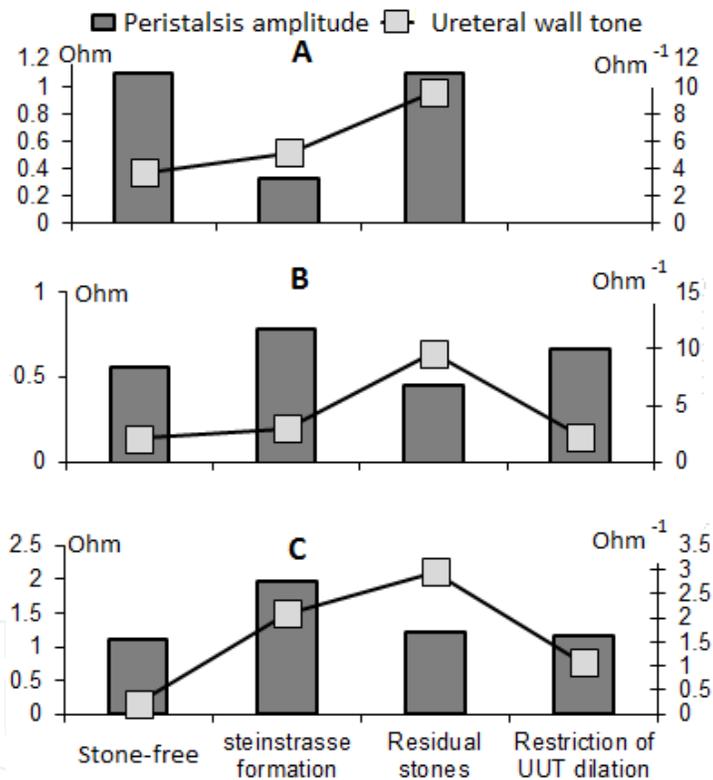


Fig. 13. Interrelation between the efficacy of a single ESWL session and UUT urodynamic status manifested by UUT dilation, and the ureteral functional characteristics. A- without UUT dilation; B- UUT dilation < 2 cm; C- UUT dilation > 2 cm

Thus, the ureteral function as well as UUT dilation are the important factors influencing stone elimination. In the patients with dilated UUT, the high amplitude of contractions can favor preservation of residual stones or contribute to steinstrasse formation promoting retrograde overshoot of the stone fragments into ureter and renal pelvis after lithotripsy (Fig. 13, C). Less efficacy of ESWL session in these patients with pronounced UUT dilation, and steinstrasse formation despite strong contractile function of their ureter can be

explained by possibility of hydrodynamic transmission of ureteral contractions in both upstream and downstream directions along the dilated and opened UUT. These results are well explained on the basis of peristaltic and diuretic mode of urine transport. It is known that during basal hydration, the process of renal pelvic filling and emptying is active, being characterised with the rhythmic pelvic contractions while stimulated diuresis triggers transition from an active to passive peristalsis mode accompanied by transmission of voiding pressures and spontaneous bladder pressures to the kidney.

So, the strong ureteral contractile activity contributed to successful stone elimination in the patients with no (33%) or moderate (33%) UUT dilation, but it accompanied the residual stone formation in the most of patients with dilated (>2 cm) UUT (70%), and in 33% patients with non-dilated UUT.

In the patients with no evident UUT dilation, the strong ureteral contractile activity promoted successful elimination of the stone fragments in the cases of low ureteral wall tone, but also accompanied the residual stone formation in the cases of elevated ureteral wall tone (Fig. 13, A). In both urodynamic conditions relating to UUT dilation, the disorders in vigorous contractile activity manifested by retrograde peristalsis clearly indicated inefficacy of stone fragments elimination treatment.

So, UUT dilation and ureteral mode of peristalsis can influence the stone free-rate after lithotripsy treatment. UUT dilation moderated pronouncedly after successful stone destruction in a 10-day period in the patients characterized with prevalence of strong antegrade contractions (1.68 ± 1.17 Ohm), while US and X-ray picture was worse in those patients who demonstrated depressed contractile activity (0.47 ± 1.14 Ohm), and dilation did not change after stone removal in the patient with aberrant (amplitude 0.08 Ohm) peristalsis evidencing functionally decompensated ureter. We can speculate that ureteric activity is essential for restoring UUT size after treatment while the normal contractile function of ureter can compensate the urodynamic disorders provoked by the stone.

7. Effect of stents on ureteral performance

Our observations of the effects of ureteral stent on the course of stone disease are based on evaluation the parameters of ureteral peristalsis in ureters immediately after being stented. Quantitative and qualitative parameters were measured in 10 patients (16 ureters) examined in dynamics, i.e. before stent indwelling and after its removing. These patients had stone disease complicated by hydronephrosis. In addition, ureters of 10 patients were examined by MIUG during ureteroscopic stent removal after clinically defined period of stent indwelling. On the whole, the effects of ureteral stenting on the ureteral peristalsis were greatly individual.

The individual mode of ureteric peristalsis depended on foregoing pathologic conditions. Analysis of the dynamic changes of ureteral peristalsis in the patients examined before stent insertion and after it withdrawn yielded some important inferences. On the whole, positive effects of ureteral stenting on urodynamic appearance were manifested with UUT dilation restriction. This effect was achieved because the procedure of stent indwelling normalized the peristalsis order and decreased the amplitude of ureteral peristalsis and the ureteral wall tone (Fig. 14). The contractile waves with pronounced slow tonic component (A) became smaller than those before stenting and free from tonic component (As). In one month after stent indwelling, the retrograde and frequent contractile waves (B) lessened (Bs). In patients

with local peristaltic abnormalities manifested by irregular contractile activity in various ureteral segments, the stent indwelling corrected the direction of ureteral peristalsis, harmonized ureteral contractions, and moderated the local peristaltic disorders.

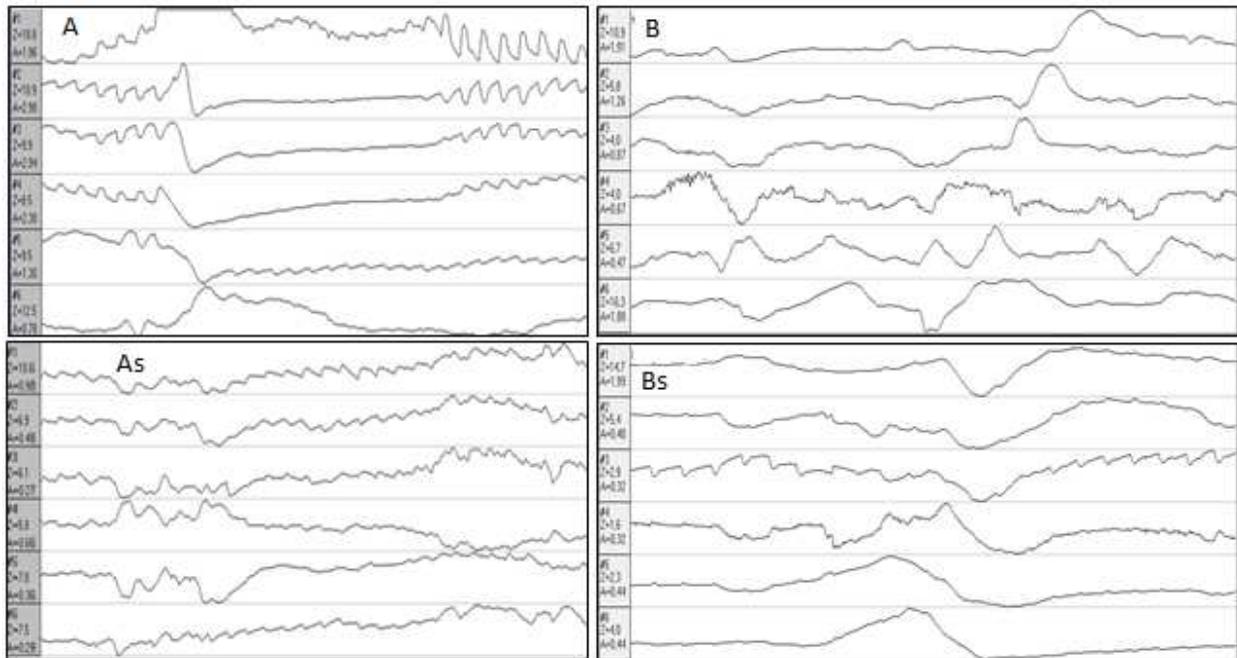


Fig. 14. Examples of ureteral peristalsis demonstrating dynamic changes after internal stenting in two patients (A, and B). A, B- records before stent indwelling; As, Bs- records immediately after stent removing; each record time is 20 sec

In the group of patients examined dynamically, the intrinsic individual mode of ureteral peristalsis preserved its original appearance, and the characteristics of ureteric function did not change significantly during the observed 1-1.5-month period of stenting. At the same time, the peristalsis amplitude and ureteral wall tone decreased in the most of patients (80%). In a small group of patients (20%), the stent indwelling augmented the ureteral peristalsis.

In the group of patients examined only once immediately after 1-1.5-months stent indwelling by MIUG, the strong peristalsis amplitude ($1.24 \pm 0.16 \text{ Ohm}$) and low ureteral wall tone ($2.22 \pm 0.63 \text{ Ohm}^{-1}$) was recorded in 5 of 10 patients observed. The rest 5 patients demonstrated weak aberrant peristalsis ($0.20 \pm 0.04 \text{ Ohm}$) and high ureteral wall tone ($6.34 \pm 1.08 \text{ Ohm}^{-1}$). The observed peristalsis characteristics may reflect different individual ureteral conditions, and different reactions to stenting.

MIUG recordings illustrate the irritation of ureteral wall after stent indwelling manifested by frequent arrhythmic bursts of bioelectrical activity that appeared periodically in various parts of the ureter. We can suppose that the stent itself acts like a stone and irritates the ureter wall stimulating the contractile activity of smooth muscles. Some ureters can react to stent indwelling by increased ureteral contractions and demonstrate hyperfunction (fig.15, A). However, some ureters are unable to respond to foreign body insertion with increased peristalsis amplitude and remained decompensated (B).

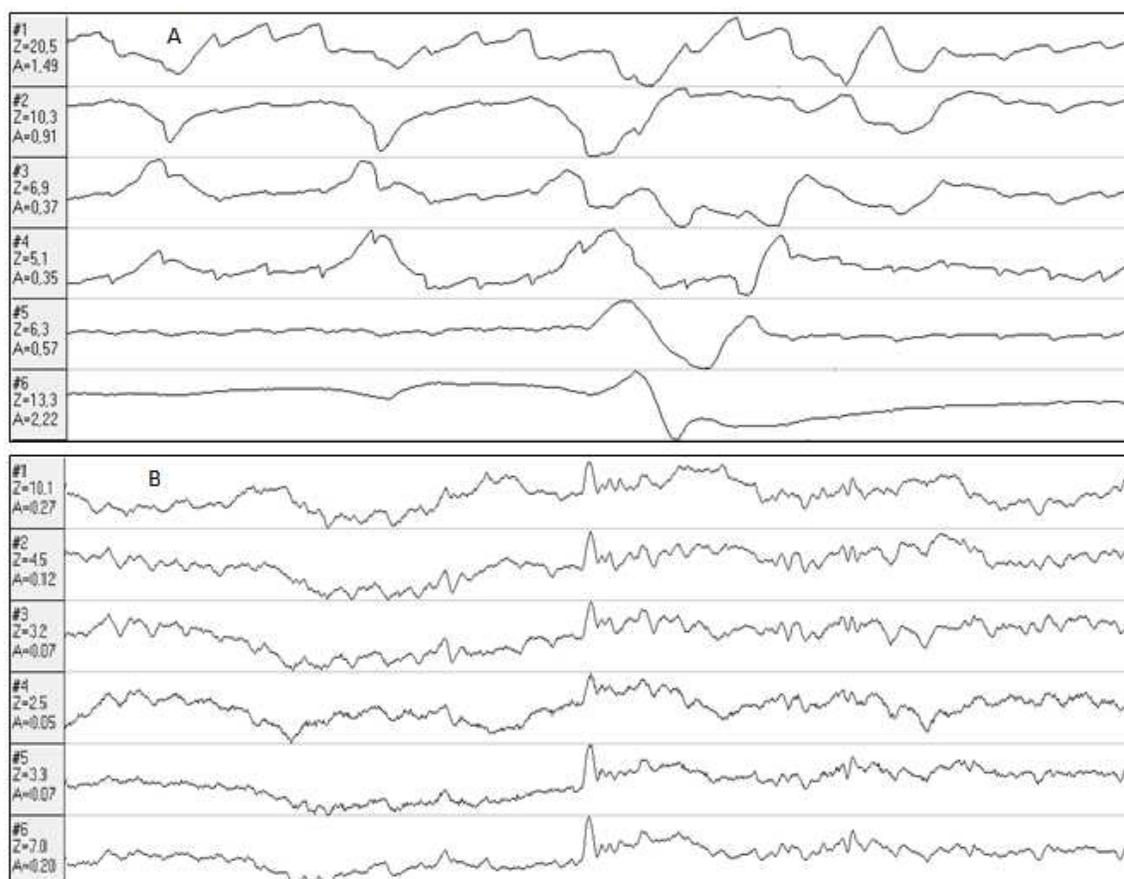


Fig. 15. Examples of ureteral peristalsis after internal stenting obtained by MIUG in two patients: A- with strong contractile activity in the ureter, and B- with weak peristalsis; each record time is 20 sec

There are still controversial opinions on the necessity of stent indwelling and corresponding indications for ureteral stenting for the patients subjected to ureteroscopy and lithotripsy (Venkatesh et al., 2005; Haleblan et al., 2008). Clinical examinations of the patients did not reveal any difference in the results of stent indwelling despite the differences in the character of the contractile function manifested by pronounced or aberrant peristalsis. In our opinion, the relief of UUT obstructive symptoms, and stabilization or improvement of renal function after stent indwelling is a likely outcome of stenting. These results were frequently observed in patients demonstrating elimination or moderation of local peristaltic disorders, the uniform peristaltic activity of ureteric regions.

The peristalsis of all ureter regions in patient with ureteropelvic junction obstruction and concomitant caluli (Fig. 16) was monitored in the 1-st City Hospital before simultaneous stone and stricture removal following by stent insertion. The pronounced peristalsis was recorded in renal pelvis above stricture region, and in middle ureter (0.88-1.15 Ohm). However, the peristaltic waves spread in opposite directions: they were constantly retrograde above the stricture region and obtained antegrade and cystoid character in the lower ureter regions. In this patient, functional peristaltic disorders were reversible, and positive results of treatment were achieved according HUN resolution and renal function restoration.

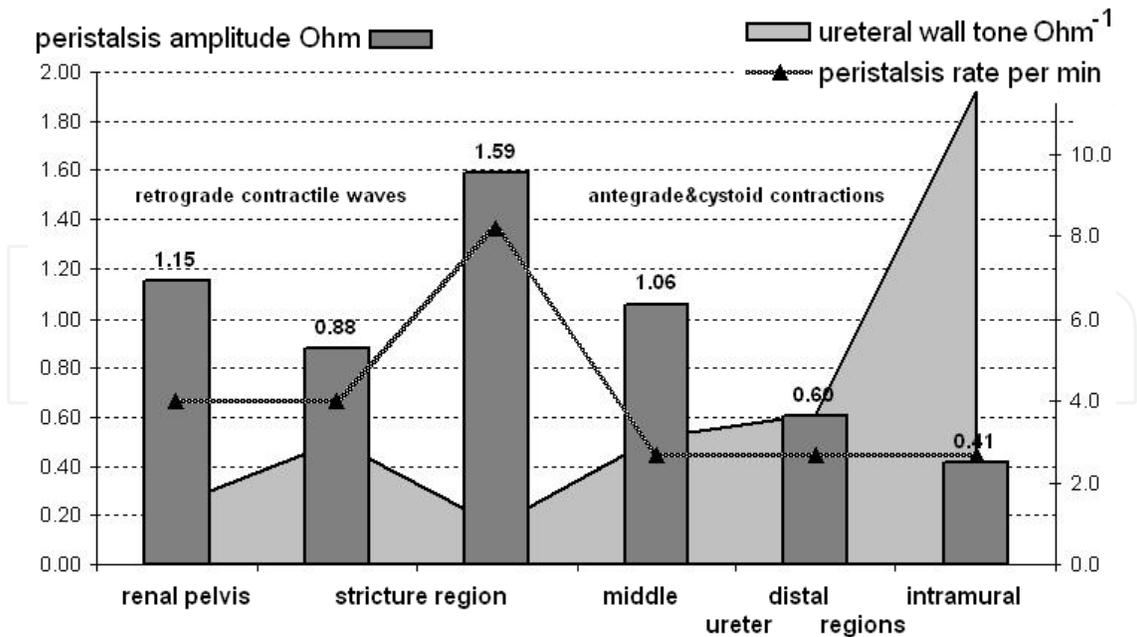


Fig. 16. Functional characteristics of the peristalsis recorded by MIUG method in different ureteral regions of a patient with ureteropelvic junction obstruction and concomitant calculi

The group of hydronephrotic patients ($n=5$) with UPJ strictures were analysed according to the parameters of ureteral peristalsis before stricture correction, and then in a 10-14 days after endoscopic treatment and immediately after stent removal (Fig. 17). Successful endoscopic treatment was marked with the following positive urodynamic changes: 1) previously reduced mean peristalsis amplitude of dilated renal pelvis and ureter increased, 2) initially high peristaltic frequency above stricture region decreased, and 3) pronounced ureteral wall tone dropped.

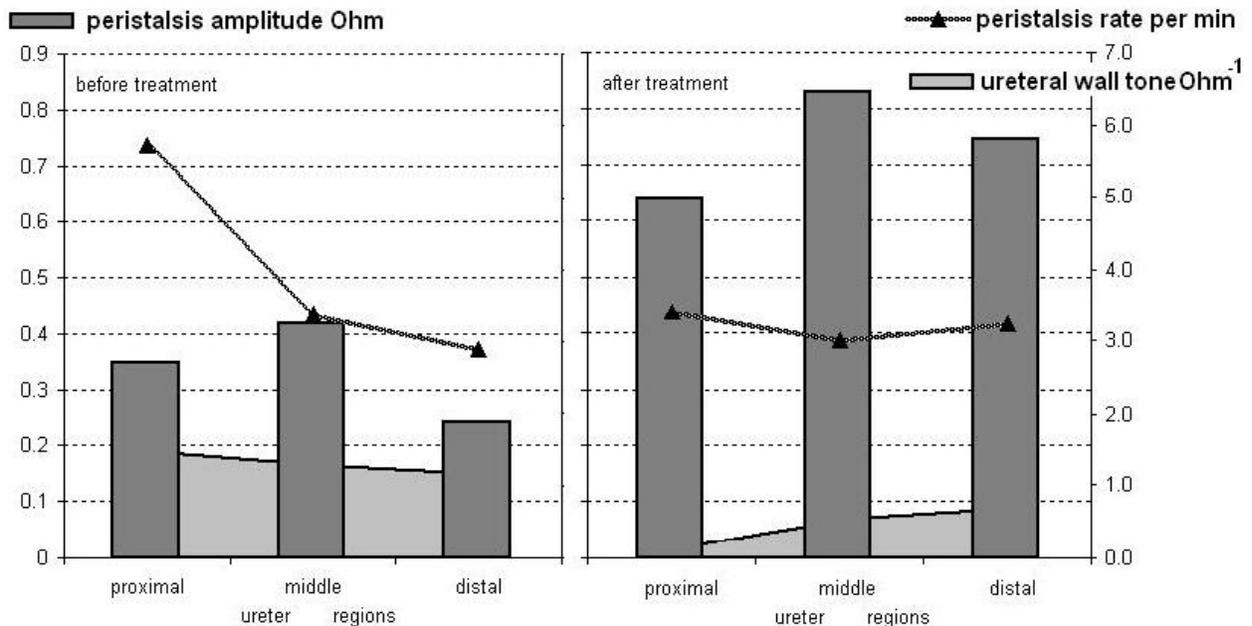


Fig. 17. Changes in ureteral function obtained with MIUG after endoscopic UPJ stricture correction and stenting in patients with hydronephrosis

When the urodynamic data obtained during the course of treatment corroborated such tendency and if the quantitative characteristics of ureteric contractile function became more uniform in different ureteral parts after the treatment, the correction was considered as successful. It was clinically approved. Moreover, qualitative features of ureteral peristalsis tended to be in order (Fig. 18): the amount of retrograde, cystoid, and aberrant arrhythmic contractile waves diminished, while normal antegrade contractions were more often observed along the ureter than before endoscopic stricture correction and stent indwelling.

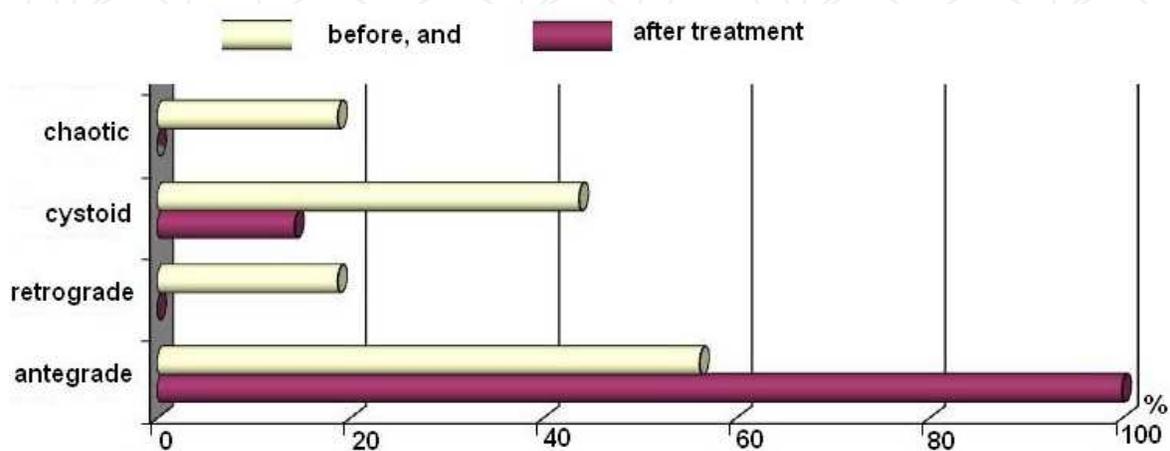


Fig. 18. Character of ureteral peristaltic waves obtained with MIUG after endoscopic UPJ stricture correction and stenting in patients with hydronephrosis

So, in hydronephrosis, the positive urodynamic changes resulted from successful treatment are the concordant uniform peristaltic activity in all ureteric regions, an increment of the amplitude of ureter contractions, a decrease in the ureteral wall tone, and a drop in the peristaltic rate, especially in the upper region of the ureter. In these cases, the signs of peristaltic orientation disorders and arrhythmia diminished.

Thus, stenting per se can be helpful to harmonization of peristaltic process in dilated ureter and reversion of the abnormal hydronephrotic changes if the intrinsic contractile compensatory reserves are safe. In so going, the normalization process might be indicative on the functional changes in the examined UUT not accompanied by severe structural lesions.

8. Peculiarities of ureteral function in patients with stones in the upper urinary tract after alpha-blocking medication

In this study, the parameters of the ureteral peristalsis and RPP values were compared in two groups of patients, respectively, who were treated with α -adrenoblocker tamsulosin (0.4 mg daily) in addition to the standard regimen, and patients without α -blocking medication. Patients in both groups (15 and 25 persons, consequently) were matched according to the size and location of the stones in UUT.

The positive effects of α -blocking were demonstrated in clinical settings with varying rate of success and the mechanism of this therapy was analyzed. In ureteral pressure measurements, a hypothesis has been advanced that reduction in pressure generation may be an essential factor promoting stone passage during α -adrenoblocking therapy

(Davenport et al., 2007). Moreover, it was suggested that these drugs work by preventing an augmented uncoordinated muscular activity whilst maintaining peristalsis, thereby promoting stone passage. Our data corroborate this hypothesis (Fig. 19).

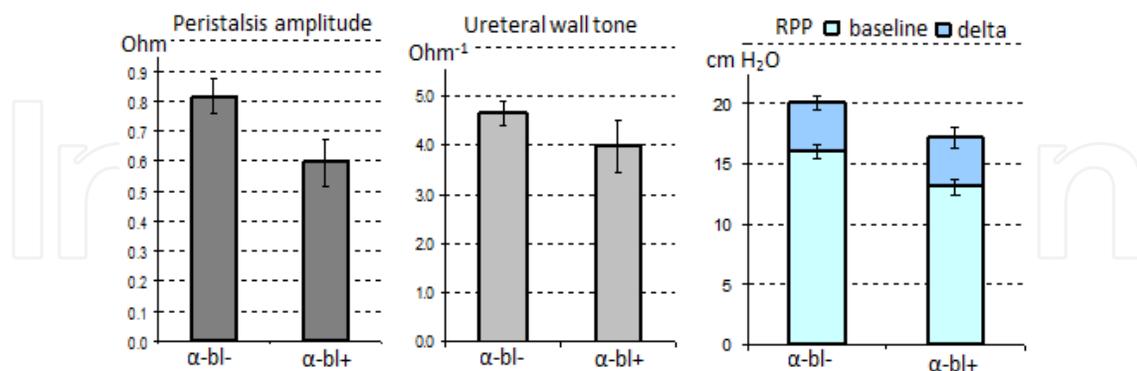


Fig. 19. Parameters of ureteral function in patients with stone disease after α -adrenoblocking therapy (α -bl+) compared to the patients without α -blocking medication (α -bl-)

In the patients receiving α -adrenoblocker, the peristalsis amplitude was weaker by 2.9 ± 3.5 Ohm ($p < 0.02$) than in patients treated according to the standard regimen, the contractions were shorter by 9% ($p < 0.1$), frequency was greater by 18% ($p < 0.1$), the ureteral wall tone was smaller by 14% ($p < 0.5$), and the normal antegrade regular contractions were more frequently (by 30%) observed. The average RPP values were smaller by 15-28% after α -adrenoblocking therapy, although diuresis via nephrostomy tubes was similar in both groups (1.1 ± 0.1 and 0.9 ± 0.1 ml/min).

Moreover, different urodynamic changes were found after α -adrenoblocking therapy in patients with proximal and distal stones in UUT (Fig. 20). In the patients with stones located in the kidney and proximal ureter, there were no significant differences in the parameters of ureteral peristalsis between the examined groups except for the lower peristalsis amplitude by 38% ($p < 0.02$) in the patients receiving α -adrenoblocker medication, and there was no intergroup difference in RPP. While in the patients with distal ureteral stones, no differences were found between the parameters of peristalsis in both groups, but RPP value was significantly smaller in the patients receiving α -adrenoblocking therapy. The baseline and peristaltic pressure was smaller in this group by, respectively, 47% and 39% compared to the patients treated according only to the standard regimen.

As discussed in the above, differently located stones in UUT could evoke different reflexes, and, therefore, different functional urodynamic changes. In view of the dominant role of adrenoceptors in ureteral function modulation, α -adrenoblocking therapy can induce urodynamic changes by this pathway. Thus, we can suppose that the renal and proximal ureteral stones can evoke reflex irritation of the excitatory adrenergic fibers in distal ureter that stimulate its contractions; therefore, α -adrenoblocker can moderate the ureteral contractions by blocking adrenergic receptors. Elevated RPP in patients with proximal stones in UUT is urodynamic in nature, i.e., it predominantly results from obstruction with a stone hindering urine outflow from the kidney. Therefore, α -adrenoblocker could not affect this parameter. In the case of distal stones, irritation of distal ureter via adrenergic excitatory mechanism can induce reflex elevation of pressure in kidney; therefore, α -adrenoblocker can induce reduction in RPP by blocking corresponding receptors.

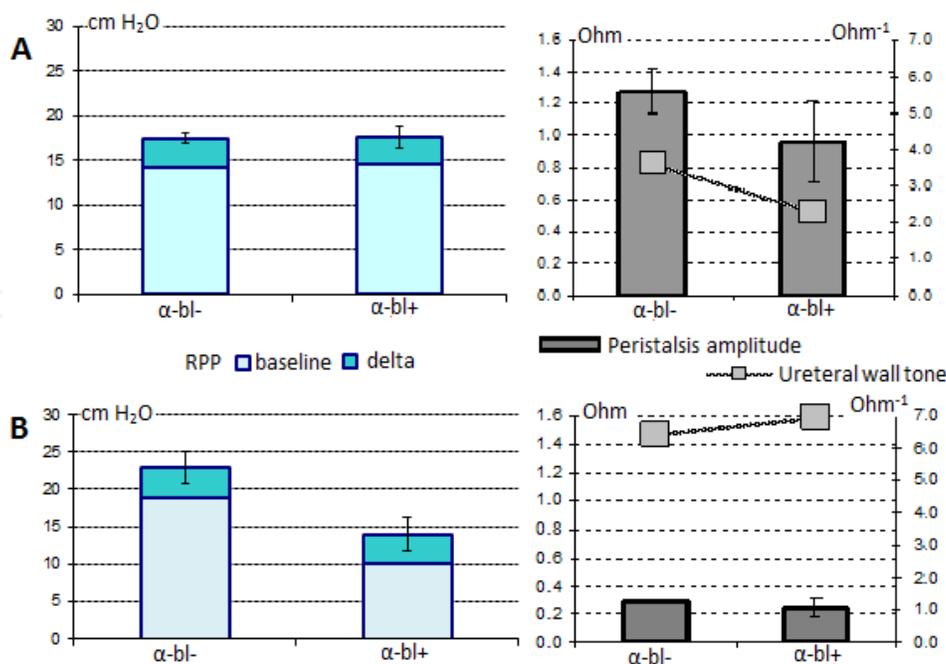


Fig. 20. Different effects of α -adrenoblocking therapy in patients with stones in kidney and proximal ureter (A), and with distal ureteral stones (B)

Individual ureteral peristalsis peculiarities mentioned above, such as pronounced contractile activity, or aberrant peristalsis, also can impress α -adrenoblocking effects on ureteric function. The patients whose ureters demonstrate aberrant peristalsis, i.e. very weak chaotic waves and high ureteral wall tone cannot response well to α -adrenoblocking therapy. We suppose that such aberrant peristalsis can result from previous general inflammatory and fibrotic changes in ureteral wall that cannot be modulated by autonomic neural influences. There were no differences between the parameters of ureteral peristalsis in such patients with or without α -adrenoblocking therapy. Their ureters do not actively participate in urine transport by peristaltic activity, urine transport in these patients is fulfilled under pressure gradient like as during diuretic flow, and therefore such ureters need to be treated by creating unobstructed low-pressure urine passage.

When patients with adequate peristaltic function were compared, the peristalsis amplitude was smaller in the patients receiving α -adrenoblocker compared to that without this medication (0.97 ± 0.25 vs 1.30 ± 0.14 Ohm), the ureteral wall tone was lower (2.30 ± 0.55 vs 3.60 ± 0.56 Ohm⁻¹), the contractions were shorter by 17% and faster by 52%, and RPP was smaller (13.50 ± 0.69 vs 22.90 ± 5.40 cm H₂O) indicating the better urine drainage from the kidney.

Thus, efficacy of α -adrenoblocker treatment can be achieved for different stone location in the upper urinary tract, but it largely depends on the individual ureter status. In patients with functional peristaltic disorders, especially with those provoked by increased adrenergic stimulation, treatment with α -adrenoblockers would be helpful in the terms of contractility normalization and ureteral wall relaxation. However, pronounced organic changes in ureteral wall caused by previous inflammatory or fibrotic processes characterized by aberrant peristalsis can be responsible for medication inefficacy.

9. Ureteral function and physiotherapy

The foregoing analysis of the ureteral peristalsis and its role for urodynamic manifestation in the course of stone disease persuade that it is essential to prevent the increased, uncoordinated contractile activity in ureter whilst maintaining normal peristalsis, thereby promoting stone passage. The application of physical factors broadened the indications for conservative therapy with patients having ureteral stones and their fragments including stainstrasse following ESWL. Our experience with one of the physiotherapeutic method based on deep oscillations of electrostatic field is supposed to be effective for stone expulsion in patients with urolithiasis.

The clinical study included 19 patients aged 39.7 ± 4.6 which were treated with various pulsed electrostatic field frequencies (I, II, and III regime): 120-180 Hz (10 minutes), 65-85 Hz (10 minutes), and 14-25 Hz (5 minutes). The minimum course of treatment consisted of 2 procedures, the maximum - consisted of 7 procedures.

Following the first procedure, 32% patients noted a decrease of pain, and steady diuresis increase was noted in 42% patients. Renal parenchyma oedema terminated in 37% patients after 3-5 procedures. Stone migration was noted in 74% patients, and 21% patients experienced renal colic attacks with the successive spontaneous stone passage (Fig.21). Concrement elimination has made up 86% with stones ≤ 5 mm; 73% with stones 5-10 mm; and 83% with steinstrasse length up to 10 mm. One patient was excluded from the study because of pyelonephritis attack development following the first procedure. On the whole, the treatment had no effect on the recovery in 21% patients.

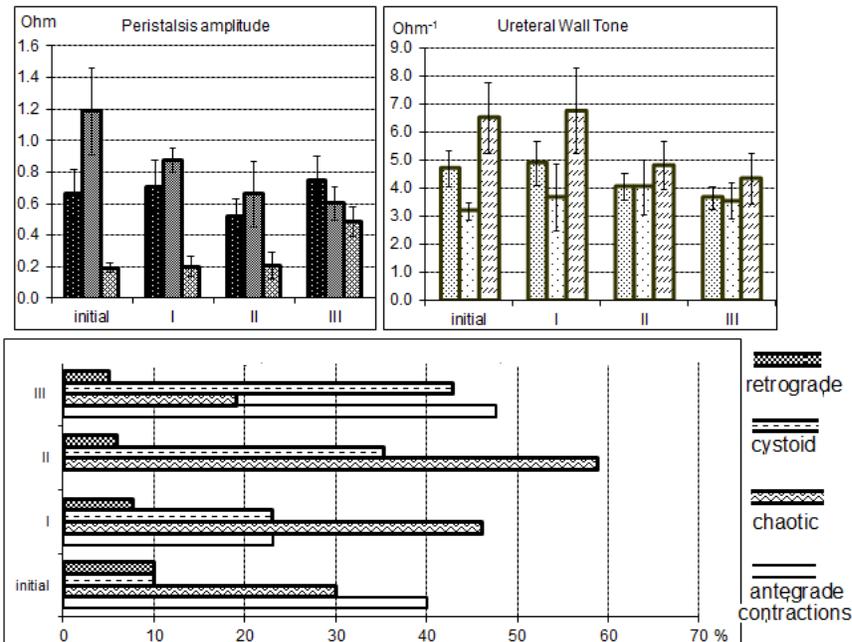


Fig. 21. Distribution of patients with stone disease according to clinical effects of physiotherapy

Concerning these favouring clinical results, acute effects of this physiotherapy on ureteral function were assessed for 8 patients undergoing ureteroscopy by MIUG method. Two

external electrodes were applied on the front abdominal wall in projection of ureter, and diagnostic probe was installed into a distal ureter. The ureteral peristalsis has been monitoring during 3-minute period initially, and then within each physiotherapeutic regime.

The overt effects of examined physical factors were documented by immediate changes in peristalsis amplitude, peristalsis rate, ureteral wall tone, and the character and direction of contractile waves travelling along the ureter. These parameters of ureteric contractile function changed individually in patients depending on the frequency of applied electrostatic field and initial ureter status (Fig.22).

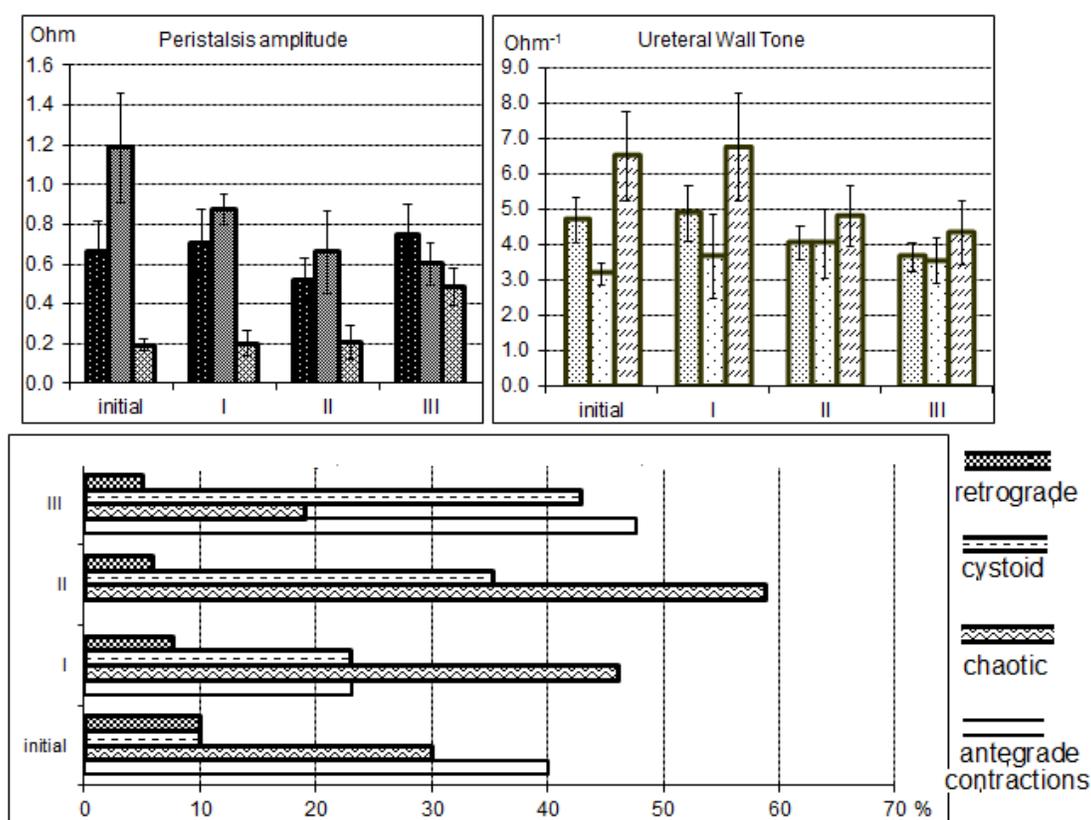


Fig. 22. Dynamic changes in the peristalsis amplitude, ureteral wall tone, and contractile wave characteristics within three (I, II, and III) applied physiotherapeutic regimes. Consecutive columns describe the changes in peristalsis amplitude and ureteral wall tone in different patient groups, respectively, all 8 patients examined, patients with initially strong contractile activity in ureter, and patients with aberrant ureteral peristalsis

On the whole, peristalsis rate increased at all frequencies by 30-50%. The ureteral wall tone decreased by 14% and 22% ($p < 0.001$) in response to electrostatic oscillations at frequencies 85 and 180 Hz, respectively. The chaotic contractions frequently (30%) observed prior to physiotherapy were replaced by antegrade (48%) or cystoid (43%) peristalsis accompanied by an inhibition of retrograde contractions. No average significant changes were noted for the peristalsis amplitude, however, it has been changing depending on initial conditions with individual patients. The strong initially contractions used to decrease after physiotherapeutic stimulation, while weak contractile activity used to enhance in patients with aberrant peristalsis.

These findings suggest that physiotherapy is capable to affect the ureteral contractile function by normalizing the character of its peristalsis, decreasing ureteral wall tone, and individually stimulating the weak ureteral contractions or decreasing strong retrograde contractile waves. The energy of deep oscillation with electrostatic field can induce changes evidencing to spasmolytic, and diuretic effects of this procedure. In complex lithokinetic therapy of patients with stone disease, physiotherapy can be helpful in facilitating stone evacuation, and restoration of urine passage due to improved diuresis. It is likely this procedure in some cases can replace medication.

10. Conclusion

Physiology of UUT established an important role of ureteral function in the process of urine transport from kidney to the urinary bladder. A lot of experimental studies have described the role of ureter in the urodynamic processes under the normal and pathologic conditions. In clinical settings, less information is available to reliably reflect the ureter function relating to urodynamic disorders because the technique is still invasive and necessitates ureter catheterization. Despite these instrumental difficulties, the functional urodynamic studies on UUT urodynamics have been carried out in patients with stone disease using the intraluminal pressure measurements and videourodynamic technique. At present vital importance of functional urodynamic diagnostics of UUT is evident. Based on numerous experiments on animals, we developed a multichannel impedance technique to observe the peristalsis along the ureter in urological patients concurrently with the standard US and X-ray examinations.

Evaluation of the ureteral peristalsis by multichannel impedance ureterography (MIUG) provides supplementary diagnostic tools important both for clinical practice and for understanding the mechanisms of urodynamic disorders in patients with stone disease. This method yields relative quantitative and qualitative data on ureteral peristalsis and reveals individual peculiarities in the patients. This method can be useful when choosing a medical treatment for an individual patient, and can predict the efficacy of treatment in the course of stone disease.

Undoubtedly, individual ureteral functional peculiarities play specific role in stone disease course, and they must be taken into consideration in the course of treatment.

The strong contractile activity can play the double role in the process of stone passage after ESWL. It was shown to be a facilitating factor, if contractions spread antegradely towards a bladder through the dilated or undilated UUT. But in the dilated UUT, complications like residual stone fragments and steinstrasse formation are quite possible, especially in case of strong retrograde and uncoordinated contractions.

Strong contractile activity in ureter is often observed in primary patients. This activity even being functionally destroyed can be easily modulated by medication, and can be reversible after emergent stone removal. But strong persistent retrograde contractions may cause urine refluxes and stagnation complicated by inflammation.

Weak contractile activity was a characteristic of ureter inherent for lot of patients with stone disease. Such aberrant peristalsis was frequently seen in patients with long history of stones in UUT. Also, aberrant peristalsis and high ureteral wall tone was observed in place of the stone or stricture location. Patients with such mode of peristalsis usually need long period to

rehabilitate the UUT urodynamics after lithotripsy procedures. Stents might be helpful in treatment of the peristalsis disorders in dilated UUT.

The quantitative parameters of UUT peristalsis obtained by MIUG that give worse treatment results in combination with the qualitative features are:

- weak UUT peristaltic activity + high ureteral wall tone,
- strong ureteral contractions + retrograde peristaltic waves.

These ureteral functional characteristics are shown to be the reason of RPP elevation evidencing to inadequate renal drainage.

The renal pelvis pressure is a complex urodynamic parameter. A lot of factors are responsible for RPP elevation that would produce a harmful effect on renal function. There are no doubts that the main players here are obstruction and inflammation. The quicker removal of obstruction and rapid elimination of inflammation mean better restoration of pelvic pressure. Also, elevation in interstitial pressure due to continuing pathologic process in renal parenchyma, and inadequate ureteral function that must provide urine outflow from kidney can be additional factors responsible for moderately increased pressure in renal pelvis after elimination of the main factors.

Thus, ureteral peristalsis and RPP are valuable indicators of functional UUT urodynamic disorders. Assessment of these functional parameters in different patients under various clinical situations persuades us that except the general changes typical of disease and treatment modality, the individual functional features are attended anytime and anywhere. Therefore, the parameters of ureteral function and pressure in renal pelvis are likely to be controlled in the course of disease. Individual evaluation of these UUT urodynamic characteristics might be useful in definition whether patient will respond to medication and conservative treatment, or more invasive management is indicated.

11. Acknowledgment

We are indebted to many people for their help with the complex urodynamic examination of patients with stone disease upon which this article is based. We would like to thank Mr. Martov Aleksey G., Mr. Moskalenko Sergey A., Mr. Fachretdinov Gennadiy. of the Moscow Urological City Hospital N. 47, and Mr. Dzeranov Nikolay K. & Mr. Beshliev Djamaal A. of the Moscow Research Institute of Urology in whose departments the major part of this work was carried out. On the technical side I am grateful to Mr. Revenko Sergey V. who has given me encouragement, advice, and invaluable assistance.

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