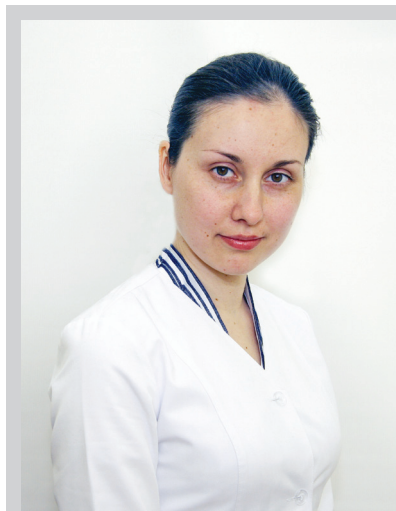


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# ANALYSIS OF URODYNAMIC INDEXES IN PATIENTS WITH INFILTRATIVE CERVICAL CANCER AFTER NERVE-SPARING RADICAL HYSTERECTOMY



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**Key Words:** infiltrative cervical cancer, nerve-sparing radical hysterectomy, cystomanometry.

**Aim** — to evaluate contractile function of urinary bladder in patients with infiltrative cervical cancer (CC) after nerve-sparing radical hysterectomy (NSRH). 90 patients with infiltrative CC were treated with NSRH (n=45), or radical hysterectomy III type (RHE III) without preservation of pelvic autonomic plexuses (n=45). While at preoperative period P1 indexes did not differ significantly between the groups, after NSRH performance, P1 values were significantly higher than P1 values in the group of patients treated with RHE III ( $8.29 \pm 1.1$  vs  $3.51 \pm 0.8$  cm H<sub>2</sub>O;  $p < 0.05$ ). P2 indexes in patients from both groups before and after surgical treatment differed significantly and were  $6.82 \pm 0.4$  and  $12.27 \pm 1.2$  cm H<sub>2</sub>O ( $p < 0.05$ ) in NSRH group, and  $5.44 \pm 0.6$  and  $10.62 \pm 1.1$  cm H<sub>2</sub>O ( $p < 0.05$ ) in RHE III group. The P value in both patients groups before and after the surgical treatments was significantly different, and demonstrated a gradual elevation of urinary bladder pressure, especially in the patients from RHE III treated group. Urinary bladder volume at preoperative and postoperative periods in NSRH-treated group remained practically unaltered ( $209.78 \pm 14.2$  and  $216.86 \pm 14.9$  ml ( $p > 0.5$ ) respectively), while in the patients from RHE III-treated group after surgical treatment an urinary bladder volume significantly decreased from  $188.4 \pm 10.5$  to  $161.9 \pm 9.8$  ml ( $p < 0.05$ ). The data of urodynamic study evidence on better preservation of urinary bladder functions in patients with infiltrative CC after NSRH than in the patients treated with RHE III.

## INTRODUCTION

In last years, a significant progress in the treatment of cervical cancer (CC) has been achieved. New methodological principles have been developed and applied, and equipment and surgical techniques have been improved. In locally-advanced forms of CC, urinary system could be involved in pathological process in 50% of cases [8, 10, 11] due to a close anatomic allocation, common sources of blood supply and innervation of pelvic organs [1, 6, 9, 15]. Sometimes, the results of surgical treatment could be dissatisfactory. Among the causes of such insufficiency one should mention various urologic complications including inflammatory diseases of urinary system, urolepsia, decreased bladder capacity [3, 7, 15, 16]; complications caused by trauma and denervation of urinary organs during surgery of pelvic neoplasms [2, 5, 12, 17].

At early stages of cancer development, functional changes in urinary system accompanied with morphological changes could be observed. Foremost, such anatomic-functional changes result from close anatomic-topographic relations. Ureters kinking over *linea innominata*, pass along lateral pelvic wall. Their terminal parts are located in *trigonum vesicae* region. The distance between urinary bladder and anterior wall of vagina does not exceed 1.5–2 cm. The

region of *trigonum vesicae* corresponds to upper and partially middle third of anterior wall of vagina, while upper departments of bladder adjoin endocervix. They are separated with fibrous tissue which forms vesicovaginal septum.

Lateral walls of urinary bladder are located close to mesodesma, and urethra makes contact with lower third of vagina. An extension of tumor process from uterus, uterine adnexa and vagina into urinary organs is facilitated with common sources of innervation, blood- and lymph-circulation. Even small tumor may cause certain anatomic-topographic alterations in urinary organs via reflectory or local toxic action. Malfunction of lymphatic or arterial systems cause degenerative changes in nerve elements thus promoting the development of hydroureteronephrosis. Obstruction of ureters is often observed in the places of location of the most functionally active nerve apparatus — in intramural and juxtavesical regions. Traumatic injury of neuroangliac apparatus of ureters during surgery of CC plays a role in the development of urinary stasis.

Before surgery it is important to evaluate an anatomic-functional state of urinary system. Also, urologic examination should be performed in the process of therapy and during dynamic monitoring of the patients. This is the only way

to reveal the initial stages of injury of urinary organs in the patients with CC, to understand their character and causes and to propose a correct curative tactics. Ultrasonic and urodynamic methods play a central role in diagnostics of malignant tumors of lower pelvis and allow detect alterations in urinary system before and after surgical treatment. Unfortunately, until quite recently an urodynamic study of urinary system has not been used in a complete examination of the patients with gynecological cancer. Clinical experience evidences that the severity of urologic complications increases along with tumor enlargement and expansion, and depends on the stage of the disease [4]. Independent of the disease stage, urologic study should be performed in an integrated manner and include clinical and biochemical urine and blood examination, cystoscopy, ultrasonic and urodynamic examination, as far as many patients already have significant alterations of urinary system state at preoperative stage.

**MATERIALS AND METHODS**

90 patients with infiltrative CC were treated with radical hysterectomy (RHE) in the Department of Oncogynecology of National Cancer Institute (Kyiv, Ukraine) in 2012–2016. In 45 patients (group I) RHE was performed with preservation of pelvic autonomic plexuses (nerve-sparing radical hysterectomy — NSRH), and in 45 patients RHE was performed by standard method without preservation of pelvic autonomic plexuses (group II, control group). The prognostic indexes in the groups were similar. Table 1–3 present the distribution of the patients with infiltrative CC in the groups by the main prognostic criteria.

An informed consents were obtained from patients according to the Ethical Commission requirements of the National Cancer Institute of Ukraine. Urodynamic study was carried out with a special system «Uro-Pro» (Ukraine) 1 day before the surgery and in 3–4 days after hysterectomy. Bladder wall compliance is measured as a change of detrusor pressure upon certain change of filling volume. Compliance is calculated by a formula:

$$C=V/P,$$

where P — change of detrusor pressure at a moment of change of volume. Compliance is expressed in ml/cm H<sub>2</sub>O. Normally, compliance should be higher than 10 ml/cm H<sub>2</sub>O at a volume up to 100 ml and higher than 25 ml/cm H<sub>2</sub>O at a volume up to 500 ml. If compliance is low (what is usually observed upon sharp increase of pressure and moderate volume change), it is unfavorable for the state of upper urinary tract [13].

Statistical analysis of the data was performed with the use of programs STATISTICA 5.0 for Windows, Stat Soft, Inc., USA. The differences between the groups were evaluated using parametric and nonparametric criteria using Student's *t*-criterion.

**RESULTS AND DISCUSSION**

A comprehensive urodynamic study of lower urinary tract that includes uroflowmetry, cystometry, and rectomanometry, should

be performed preoperatively and postoperatively. Urodynamic study in the patients with infiltrative CC is reasonable as far as it allow reproduce patients' symptoms, explain the mechanism of malfunction development, and reveal the most significant defects in the case of combined malfunction of lower urinary tract. Also an urodynamic study could be used for prognosis of possible failure and for finding the causes of inefficiency of an applied therapy. Among the most important urodynamic methods one could mention cystomanometry. Cystometry provides an information on adjustment of urinary bladder to the process of its filling as well as the CNS control of reflex of detrusor and sensor characteristics; it is a simple, informative and mostly important method of examination allowing reveal malfunction of bladder in cancer patients.

Cystometry (cystomanometry) is a registration of the changes of intravesicular pressure during its filling and urination. For the first time cystometry was performed in XIX century, but its clinical relevance has been established just recently due to the development of urodynamics as clinical discipline [11, 14].

During cystometry the fluctuations of intravesicular pressure in the process of bladder filling are recorded in graphic form. With the use of cystometry, we have evaluated the main urodynamic indexes such as pressure upon bladder filling (P1), first vesical tenesmus pressure (P2); change of detrusor pressure upon change

of bladder volume (P), volume of urinary bladder (V), and compliance of urinary bladder wall (C) at preoperative period and postoperative period in the groups of patients with infiltrative CC treated with RHE with preservation of pelvic autonomic plexuses (n=45), or without preservation of pelvic autonomic plexuses (n=45). The results are presented in Tables 2 and 3.

As one may see, indexes of the pressure upon bladder filling at preoperative period in the patients treated with RHE III and NSRH did not differ significantly (2.96±0.6 vs 3.80±0.68 cm H<sub>2</sub>O respectively; p>0.3). However, after NSRH performance, P1 values were significantly higher than P1 values in the group of patients treated with RHE III: 8.29±1.1 vs 3.51±0.8 cm H<sub>2</sub>O (p<0.05). So, pressure upon bladder filling significantly increased after NSRH, but not RHE, due to the preservation of vegetative innervation of urinary bladder.

Indexes of first vesical tenesmus pressure in patients from both groups before and after surgical treatment differed significantly and were 6.82±0.4 and 12.27±1.2 cm H<sub>2</sub>O (p<0.05) in NSRH-treated group, and 5.44±0.6 and 10.62±1.1 cm H<sub>2</sub>O (p<0.05) in RHE III-treated group. So, one may conclude that the type of surgical intervention has no effect in regard to first vesical tenesmus pressure, but P2 index depends on the timing of such examination.

The change of detrusor pressure upon the change of bladder volume in both patients

**Table 1.** Clinical characteristics of infiltrative CC cases

Group	Tumor stage, %						Tumor grade, %		
	1a	1b	2a	2b	3a	3b	G1	G2	G3
PHE	7	29	24	9	2	29	2.9	52.9	44.1
NSRH	–	31	29	7	–	33	6.1	42.4	51.5

**Table 2.** Comparison of pre- and post-operative urodynamic indexes in the patients treated with NSRH (n=45)

Index	M±SD	p
P1a (cm H <sub>2</sub> O)	3.80±0.63	0.001726
P1b (cm H <sub>2</sub> O)	8.29±1.07	
P2a (cm H <sub>2</sub> O)	6.82±0.699	0.0005
P2b (cm H <sub>2</sub> O)	12.27±1.22	
Pa (cm H <sub>2</sub> O)	3.02±0.245	0.009251
Pb (cm H <sub>2</sub> O)	3.98±0.28	
Va (ml)	209.78±14.2	0.552150
Vb (ml)	216.86±14.9	
C1a (ml/cm H <sub>2</sub> O)	84.23±8.01	0.006682
C2b (ml/cm H <sub>2</sub> O)	64.22±6.83	

P1 – pressure upon bladder filling; P2 – first vesical tenesmus pressure; P – change of detrusor pressure at a moment of change of a volume; V – volume of urinary bladder; C – compliance of urinary bladder wall; each index is measured at preoperative period (a) and postoperative period (b).

**Table 3.** Comparison of pre- and post-operative urodynamic indexes in the patients treated with RHE (n=45)

Index	M±SD	p
P1a (cm H <sub>2</sub> O)	2.96±0.62	0.50159
P1b (cm H <sub>2</sub> O)	3.51±0.757	
P2a (cm H <sub>2</sub> O)	5.4±0.649	0.00001
P2b (cm H <sub>2</sub> O)	10.6±1.12	
Pa (cm H <sub>2</sub> O)	2.5±0.207	0.00000
Pb (cm H <sub>2</sub> O)	7.7±0.866	
Va (ml)	188.4±10.5	0.02466
Vb (ml)	161.9±9.82	
C1a (ml/cm H <sub>2</sub> O)	93.4±7.84	0.00000
C2b (ml/cm H <sub>2</sub> O)	26.0±1.64	

P1 – pressure upon bladder filling; P2 – first vesical tenesmus pressure; P – change of detrusor pressure at a moment of change of a volume; V – volume of urinary bladder; C – compliance of urinary bladder wall; each index is measured at preoperative period (a) and postoperative period (b).

groups before and after the surgical treatments was significantly different:  $3.02 \pm 0.2$  and  $3.98 \pm 0.28$  cm H<sub>2</sub>O ( $p < 0.05$ ) in NSRH-treated group, and  $2.5 \pm 0.2$  and  $7.7 \pm 0.8$  cm H<sub>2</sub>O ( $p < 0.05$ ) in RHE III treated group. So, these results indicated a gradual elevation of urinary bladder pressure, especially in the patients from RHE III treated group, what evidenced on lower antiperistalsis of urinary bladder wall in this group due to transection of elements of ganglia of pelvic autonomic plexuses.

An analysis of the indexes of urinary bladder volume (V) at preoperative and postoperative periods has revealed the following tendency: in NSRH-treated group V values remained practically unaltered after the surgery ( $209.78 \pm 14.2$  and  $216.86 \pm 14.9$  ml ( $p > 0.5$ ), respectively), while in the patients from RHE III-treated group after surgical treatment an urinary bladder volume significantly decreased from  $188.4 \pm 10.5$  to  $161.9 \pm 9.8$  ml ( $p < 0.05$ ). These data allow conclude that the preservation of bladder ramous of pelvic vegetative ganglia in NSRH-treated patients improves the stability of bladder volume, while the transaction of pelvic vegetative ganglia in RHE III treated patients leads to a decrease of bladder volume.

An analysis of complience of urinary bladder wall (C) has shown that af-

ter surgical treatment C indexes tended to decrease in both groups of patients:  $84.23 \pm 8.0$  vs  $64.22 \pm 6.8$  ( $p < 0.05$ ) in NSRH-treated group;  $93.42 \pm 7.8$  vs  $26.04 \pm 1.6$  ( $p < 0.05$ ) in RHE III-treated group, but in the case of NSRH the decrease is notably lower than in the case of RHE (by 20 and by 67 ml/cm H<sub>2</sub>O, respectively). So, preservation of pelvic vegetative ganglia much better preserved a complience of urinary bladder wall than RHE with transection of elements of ganglia of pelvic autonomic plexuses, thus decreasing the rate of complications developing in urinary system at postoperative period. In conclusion, the data of urodynamic study performed at preoperative and early postoperative period have shown that surgical treatment of patients with invasive CC with preservation of the major elements of pelvic vegetative ganglia allows significantly decrease the percent of postoperative complications of urinary system.

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Аналіз уродинамічних показників у хворих на інфільтративний рак шийки матки після нервозберігаючої радикальної гістеректомії

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**Резюме.** Мета — оцінити скоротливу функцію сечового міхура у хворих на інфільтративний рак шийки матки (РШМ) після нервозберігаючої радикальної гістеректомії (НРГЕ). 90 пацієнток з інфільтративним РШМ були розподілені на 2 групи: I (основна) група — 45 хворих, яким виконана НРГЕ, II (контрольна) група — 45 хворих, яким виконана радикальна гістеректомія III типу (РГЕ III) без збереження тазового вегетативного нервового сплетення. У доопераційний період Р1 істотно не відрізнявся між групами. Після виконання НРГЕ показники Р1 були значно вищими порівняно з показниками Р1 у групі пацієнтів із РГЕ III ( $8,29 \pm 1,1$  проти  $3,51 \pm 0,8$  см вод. ст.;  $p < 0,05$ ). Р2 у пацієнток обох груп до та після хірургічного лікування значно відрізнялися і становили  $6,82 \pm 0,4$  і  $12,27 \pm 1,2$  см вод. ст. ( $p < 0,05$ ) у групі НРГЕ відповідно та  $5,44 \pm 0,6$  і  $10,62 \pm 1,1$  см вод. ст. ( $p < 0,05$ ) у групі РГЕ III відповідно. Показники Р в обох групах хворих до і після хірургічного лікування значно відрізнялися і показали поступове підвищення Р, особливо у пацієнтів із РГЕ III. У до- і післяопераційний періоди у хворих із НРГЕ залишився практично незмінним ( $209,78 \pm 14,2$  і  $216,86 \pm 14,9$  мл ( $p > 0,5$ ) відповідно), тоді як у пацієнтів із РГЕ III V значно знизився з  $188,4 \pm 10,5$  до  $161,9 \pm 9,8$  мл ( $p < 0,05$ ). Отже, показники скорочувальної функції детрузора у хворих після виконання НРГЕ кращі, ніж у хворих після РГЕ III, без збереження елементів тазового вегетативного нервового сплетення.

**Ключові слова:** інфільтративний рак шийки матки, нервозберігаюча радикальна гістеректомія, цистоманометрія.

Анализ уродинамических показателей у больных инфильтративным раком шейки матки после нервосохраняющей радикальной гистерэктомии

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**Резюме.** Цель — оценить сократительную функцию мочевого пузыря у больных инфильтративным раком шейки матки (РШМ) после нервосохраняющей радикальной гистерэктомии (НРГЭ). 90 пациенток с инфильтративным РШМ были распределены на 2 группы: I (основная) группа — 45 пациенток, которым выполнена нервосохраняющая радикальная гистерэктомия (НРГЭ), и II (контрольная) группа — 45 пациенток, которым выполнена радикальная гистерэктомия III типа (РГЭ III) без сохранения тазового вегетативного нервного сплетения. В дооперационный период Р1 существенно не отличалось между группами. После выполнения НРГЭ показатели Р1 были значительно выше по сравнению с показателями Р1 в группе пациентов с РГЭ III ( $8,29 \pm 1,1$  против  $3,51 \pm 0,8$  см вод. ст.;  $p < 0,05$ ). Показатели Р2 у пациенток обеих групп до и после хирургического лечения значительно отличались и составляли  $6,82 \pm 0,4$  и  $12,27 \pm 1,2$  см вод. ст. ( $p < 0,05$ ) в группе НРГЭ и  $5,44 \pm 0,6$  и  $10,62 \pm 1,1$  см вод. ст. ( $p < 0,05$ ) в группе РГЭ III соответственно. Показатели Р в обеих группах больных до и после хирургического лечения значительно отличались и показали постепенное повышение Р, особенно у пациентов с РГЭ III. В до- и послеоперационный периоды у больных с НРГЭ остался практически неизменным ( $209,78 \pm 14,2$  и  $216,86 \pm 14,9$  мл ( $p > 0,5$ ) соответственно), в то время как у пациентов с РГЭ III V значительно снизился с  $188,4 \pm 10,5$  до  $161,9 \pm 9,8$  мл ( $p < 0,05$ ). Таким образом, показатели сократительной функции детрузора у больных после выполнения НРГЭ лучше, чем у больных после РГЭ III без сохранения элементов тазового вегетативного нервного сплетения.

**Ключевые слова:** инфильтративный рак шейки матки, нервосохраняющая радикальная гистерэктомия, цистоманометрия.