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ORIGINAL ARTICLE

Urinary tract morbidity after nerve-sparing radical hysterectomy in women with cervical cancer

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Abstract

Introduction and hypothesis Nerve-sparing radical hysterectomy (NSRH) has been developed as a method of cervical cancer treatment to reduce surgical morbidity compared with radical abdominal hysterectomy. The aim of this study was to analyze the short- and long-term effects of NSRH on urinary tract function.

Methods A study group of 117 patients underwent NSRH type C1 with pelvic lymphadenectomy for cervical cancer stages IB1–IB2 without adjuvant radiotherapy at our department. A total of 106 patients aged 21–74 years (mean age 44.8) were available for follow-up at 1 year after surgery. A transurethral catheter was left in place for 48 h after surgery, and the postvoid residual (PVR) volume was measured after its removal. One week before surgery and 12 months after NSRH, lower urinary tract function was evaluated by an urodynamic examination.

Results Five days after surgery, the PVR volume was greater than 100 ml in 5 patients (4.7%) and a suprapubic catheter was inserted into these women for bladder training over the following days. Within 14 days after surgery, urination without PVR was achieved in all women who underwent surgery. Postoperatively, a slight increase in the average maximum bladder cystometric capacity was recorded from 420 to 445 ml (p value 0.009) without prolonging the voiding time. Other urodynamic parameters were not significantly different before and 12 months after NSRH.

Conclusions In this series, NSRH preserved voiding function and bladder sensation at 1 year and did not appear to compromise oncological outcome.

Keywords Bladder dysfunction · Cervical cancer · Nerve-sparing radical hysterectomy · Postvoid residual · Urinary incontinence · Urodynamic study

Introduction

The results of both surgery and radiotherapy are comparable for the treatment of the early stages of cervical cancer, but surgical treatment is the favored modality, especially in young women. Neoadjuvant and adjuvant chemotherapy are used in individual cases based on the stage of cervical cancer. High curability rates in women in the early stages of this disease (88–97%), which are based on individualized therapy, currently emphasize the increase in the quality of life of treated women [1]. Morbidity related to the treatment of cervical cancer is specifically linked to the radical nature of the surgery.

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Bladder dysfunction is one of the most common long-term complications after radical abdominal hysterectomy (RAH) and has an incidence of 8–85% [2]. The most common disorders of RAH include loss of sensation, hypertonic urinary bladder, hypo-/acontractile bladder, urgency and stress urinary incontinence [3]. Voiding disorders have been related to damage of the hypogastric nerves and of the inferior hypogastric plexus due to radical resection of the parametrial tissue [4]. The autonomic fibers innervating the bladder can be disrupted at several stages during RAH, e.g., during dissection of the presacral or superior gluteal nodes, during vaginal dissection and mobilization of the bladder, and during resection of the cardinal ligaments [2].

After radical hysterectomy, changes usually occur in two phases. The initial phase is hypertonic and is characterized by a small, usually transient, spastic bladder. During the early postoperative stage, both surgical trauma and selective denervation result in the dominance of the parasympathetic nervous system, which leads to hyperexcitability of the smooth muscle

[5]. The nature of the surgical damage seems to be decentralization of nerve stimuli rather than complete denervation. The second phase is hypotonic, which is characterized by an overdistended bladder. Nerve-sparing radical hysterectomy (NSRH) has emerged for reducing surgery-related dysfunctions without compromising oncological outcomes [6, 7]. The nerve-sparing technique includes four main steps: the preservation of the superior hypogastric plexus at the level of the presacral area during presacral lymphadenectomy; the preservation of the hypogastric nerve dorsal to the ureter and lateral to the utero-sacral ligament during resection of the utero-sacral ligaments; the preservation of the inferior hypogastric plexus during resection of the cardinal ligament, as the plexus lies dorsal to the parametrial vessels at the level of the deep uterine vein; and the preservation of the bladder branch during resection of the deep layer of the cervico-vesical ligament [4, 8].

The aim of our study was to prospectively assess the urinary tract morbidity and voiding dysfunctions in patients with a 12-month follow-up after NSRH with lymphadenectomy and to compare the postoperative results with pre-operative status.

Materials and methods

Following ethical approval and after informed consent was obtained, 137 patients with stages IB1–IB2 disease who underwent cervical cancer surgery at our obstetrics and gynecology department between January 2004 and December 2010 were included in a prospective, non-randomized study. All women underwent NSRH type C1 with pelvic lymphadenectomy and bilateral adnexectomy. The radical nature of hysterectomy at our center corresponds to the classification by Querleu and Morrow [9]. The nerve-sparing technique includes several main steps: after complete preparation of the paracervix and visualization of the hypogastric nerve branches, we preserve the bladder branch of the inferior hypogastric plexus according to radical hysterectomy classification type C1. The dorsal parametrium is transected after the dorsal segment of the autonomic nerve system has been separated. The inferior hypogastric plexus is systematically identified and preserved by transecting only the uterine branches of the pelvic plexus at the time the lateral parametrium is transected. Ventrally, the bladder branches of the pelvic plexus are preserved in the vesicovaginal ligament. Then, only the medial part of the ventral parametrium is resected, and the bladder branches of the hypogastric plexus caudal to the course of the ureter are identified and preserved.

A total of 231 radical hysterectomies for cervical cancer were performed at our department during the study period, 137 of which were NSRH (59.3%). NSRHs were performed in patients with cervical cancer stage IB1, greater than 2 cm in diameter or with tumor size greater than half of the cervical stroma, and stage IB2 with sufficient tumor regression following neoadjuvant chemotherapy. The operations were performed by four surgeons. Adjuvant radiotherapy was an exclusion criterion for participation in our study and, therefore, 20 women with NSRH and radiotherapy (14.6%) were excluded from the evaluation. Urogynecological assessment was performed 3, 6 and 12 months after NSRH. Twelve months after surgery, 106 out of 137 study group patients (77.4%) returned to our department for both clinical and urodynamic assessments. The remaining 11 patients after NSRH were repeatedly contacted by telephone and email, but because their original attitudes did not change, they refused the proposed urogynecological examination. In the study group of 106 patients, 22 women with stage IB2 disease were pre-operatively treated by neoadjuvant chemotherapy to reduce tumor volume before surgery and to reduce occurrence of metastases in regional lymph nodes. A total of 14 patients received postoperative adjuvant chemotherapy. Cisplatin and ifosfamide were used in cases of squamous-cell cancer and cisplatin with doxorubicin in adenocarcinoma cases [10].

Urogynecological examination and urodynamic assessment

Before surgery, bladder function was assessed in all patients. Pre-operative urodynamic assessment was performed 1 to 2 weeks before surgery, whereas the control urodynamic examination was performed 12–14 months after NSRH. The same urodynamic system, Solar Silver 4 T MMS (Medical Measurement Systems B.V., Enschede, Netherlands), with water-perfusion was used both before and after surgery.

A routine urodynamic assessment was performed and consisted of filling cystometry, measurement of the urethral pressure profile, and uroflowmetry. After spontaneous bladder emptying (verified by ultrasound), a three-way urethral catheter (9 French) was inserted into the bladder in the gynecological lithotomy position. The examination began with filling cystometry using a sterile water solution and a filling rate of 50 ml/min during which individual parameters were recorded. Next, a standard measurement of the urethral pressure profile parameters was performed during catheter withdrawal from the lower urinary tract. The examination was completed by urination of the bladder volume into a uroflowmeter, followed by calculation of the postvoid residual (PVR) volume. The objectification of urine leakage during stress maneuver was performed by the cough stress test in the usual manner with a standard 300-ml bladder volume.

During the initial and control examinations, gynecological examinations were performed in all patients, who were also interviewed to determine subjective micturition difficulties. The presence of stress urinary incontinence was investigated by urinary leakage during coughing, movement or exertion,

and was also based on symptomatology of bladder hyperactivity with questions about a frequent sudden unstoppable urge to urinate and nocturia. Bladder evacuation disorder was evaluated according to the question regarding the subjective sensation of prolonged urination and/or the need for pushing during urination. For stress and urge incontinence, we asked the following questions: "Do you experience leakage of urine during coughing, sneezing, laughing, or physical activities?", "Do you have the urge to urinate frequently?", and "Do you have to get up at night because of the urge to urinate?"

A transurethral catheter was inserted at the beginning of surgery and was removed 48 h after surgery in all patients. After catheter removal, the patients were instructed to urinate every 2 h; spontaneous urination was controlled and PVR was measured by ultrasound 2, 3, 4, and 7 days after surgery. Adequate voiding function was defined as uninterrupted urination with less than 100 ml PVR volume, without the need for further catheterization. In patients with inadequate urination function and a PVR of more than 100 ml, the transurethral catheter was reinserted for the next 48 h. If residual urine persisting for 5 days after the NSRH, a suprapubic catheter was introduced under local anesthesia.

Statistical analysis

A two sample *t* test was performed to evaluate differences between urodynamic study results before and after surgery.

Results

Important characteristics and surgical data of 106 women in the study group aged 21–74 years (mean age 44.8) who presented at our department for urogynecological assessment 12 months after NSRH (weight, height, body mass index [BMI], parity, tumor histological type, grade and stage, number of lymph nodes removed) are described in Table 1.

A PVR volume of urine greater than 100 ml after urethral catheter removal 48 h after surgery was detected in 22 patients (20.8%), and in these patients, the transurethral catheter was reinserted for the next 48 h. After its removal, a PVR volume of more than 100 ml persisted in 5 patients (4.7%). Therefore, a suprapubic catheter was inserted under local anesthesia in these women, after which they were discharged from the hospital. Within 14 days after surgery, urination without PVR was achieved in all women who underwent surgery.

Urodynamic parameters measured prior to surgery and after 12 months of follow-up are shown in Table 2. Postoperatively, a slight increase in the maximum cystometric capacity of the bladder from 420 to 445 ml (p value 0.009) without prolonged voiding time was recorded. Other urodynamic parameters were not significantly different before and 1 year after surgery.

Statistically significant increases were not observed in either the number of stress urinary incontinence (SUI) cases or overactive bladder (OAB) symptoms 1 year after surgery. Prior to surgery, SUI was present in 17 patients (16.0%), and at follow-up, SUI was documented in 16 women (15.1%). In 7

Table 1 Characteristics of the group of 106 patients

		Range	Percentage
Age, years, mean (SD)	44.8 (11.1)	21–74	
Weight, mean (SD), cm	70.7 (15.4)	45–128	
Height, mean (SD), kg	165.7 (6.2)	148–180	
BMI, mean (SD)	24.8 (4.3)	17.15–39.51	
Parity, mean (SD)	2.1 (0.87)	0–5	
Histopathology, number of cases, %			
Spinocellular carcinoma	78		73.6
Adenocarcinoma	28		26.4
Tumor grade, number of cases			
1	19		17.9
2	52		49.1
3	35		33.0
FIGO tumor stage, number of cases			
IB1	66		63.3
IB2	40		37.7
Median number of LN removed (SD)	26.7 (8.79)	19–42	
Neoadjuvant chemotherapy	22		20.8
Adjuvant (postoperative) chemotherapy	14		13.2

BMI body mass index (kg/m^2), *LN* lymph nodes, *FIGO* International Federation of Gynecology and Obstetrics, *SD* standard deviation

Table 2 Urodynamic study in 106 patients: average values

	Before surgery	SD	After surgery	SD	*p* value
Filling cystometry					
First desire to void (ml)	244.75	81.64	243.85	84.99	0.963
Normal desire to void (ml)	351.42	85.29	356.23	85.19	0.687
MCC (ml)	420.01	88.57	445.38	78.71	0.009
BC (ml/cmH_2O)	93.4	9.3	89.9	6.2	0.235
Pressure-flow study					
MUCP (cmH_2O)	58.73	28.06	59.27	25.71	0.684
FUL (mm)	28.29	11.71	27.38	11.76	0.523
Uroflowmetry					
MFR, mean, ml/s	26.03	11.22	27.25	11.06	0.121
Time to MFR (s)	18.12	39.71	18.50	52.15	0.959
Voided volume (ml)	439.56	117.25	445.01	104.56	0.916
Voiding time (s)	44.12	24.37	41.39	21.46	0.283
Qmean (ml/s)	13.72	7.18	14.40	6.29	0.242

MCC maximum cystometric capacity, *BC* bladder compliance, *MFR* maximum flow rate, *MUCP* maximal urethral closing pressure, *FUL* functional urethral length, *Qmean* average flow rate, *SD* standard deviation

women, the symptoms of SUI disappeared after NSRH, whereas the symptoms appeared de novo in 6 patients. OAB was present in the same 4 women (3.8%) before and after NSRH (Table 3).

The average BMI in women with stress urinary incontinence was 24.8 (SD 4.33). The average BMI in women with symptoms of overactive bladder was 29.2 (SD 4.76), which is almost significantly different compared with the mean BMI of the whole study group (*p* value 0.05).

In 1 patient, iatrogenic injury of the ureter (0.9%) was revealed on the 7th postoperative day by intravenous urography, which is a routine part of our follow-up protocol after NSRH. No recurrent lower urinary tract infections were reported during the 12-month follow-up. None of the patients in our study experienced cervical cancer relapse 1 year after surgery.

Table 3 Urinary incontinence before and 1 year after surgery in the group of 106 patients

		n	Percentage
Stress urinary incontinence	Before surgery	17	16.0
	After surgery	16	15.1
	Disappeared	7	6.6
	De novo	6	5.7
Overactive bladder	Before surgery	4	3.8
	After surgery	4	3.8
	Disappeared	0	0
	De novo	0	0

n number of cases

Discussion

In our study, the duration of the initial postoperative bladder transurethral catheterization (48 h) in patients after NSRH was significantly shorter than in other studies, where it ranges from 7 to 14 days [6, 11–13]. Similar satisfactory results were presented by Turnbull et al. in a smaller group of 30 women after RAH with urethral catheter removal within 48–72 h after surgery. Only 17.2% of patients required recatheterization because of a PVR volume greater than 100 ml [14]. On the contrary, shorter postoperative catheterization (24–72 h) was used by Campbell et al. after laparoscopic radical hysterectomy. A higher rate of voiding dysfunctions (44%) in their study group was explained by catheter removal on the 1st postoperative day in 18% of patients [15].

Based on our results and those of some other studies, early postoperative urethral catheter removal (48–72 h) after radical surgery for cervical cancer is not associated with increased lower urinary tract morbidity [14, 15]. Compared with prolonged indwelling catheterization, early catheter removal is associated with faster return of normal bladder function and a reduced risk of lower urinary tract infection [16].

Postoperative urinary tract infection (UTI) is an independent risk factor for inadequate voiding function after NSRH, which implies that prevention, early diagnosis and treatment of urinary tract infections during the pre-, peri-, and postoperative periods are important to the promotion of early resumption of bladder function following NSRH. In patients without pre-existing urinary tract infections, the method and duration of postoperative bladder drainage could influence the risk of postoperative UTI [13].

Despite the frequency of urinary tract dysfunction following RAH, no consensus has been established on the appropriate management for its prevention in the postoperative period. Permanent and intermittent transurethral catheterization has traditionally been used to facilitate postoperative bladder drainage following RAH, but suprapubic catheterization should be the preferred method because of its distinct advantages. Wells et al. described that after RAH for early-stage cervical cancer, suprapubic catheterization is associated with an eight times lower rate of postoperative UTI and earlier training of voiding than in transurethral catheterization [16]. When a need for long-term catheterization arises, suprapubic drainage of the bladder should be the preferred method because it is superior to indwelling urethral catheterization in terms of the reduction of asymptomatic bacteriuria and the risk of recatheterization. Intermittent catheterization is associated with a reduction in symptomatic UTI compared with indwelling urinary catheterization [17]. The specific benefits of suprapubic bladder drainage are ease of use by the patient and the possibility of easy PVR volume measurement.

For postoperative management of micturition in women after radical hysterectomy, lower urinary tract function before surgery should be considered. Pre-operative functional disorders of the lower urinary tract and abnormal results in urodynamic examination should be considered risk factors for postoperative problems with evacuation of the bladder and continence [18].

The prevalence of postoperative urinary retention could also be influenced by the definition of PVR. We defined abnormal PVR volume as greater than 100 ml. The definition of abnormal PVR varies according to different authors from 50 ml [19], to 100 ml [11, 14], to 150 ml [15], to 200 ml [12]. The main result of inappropriate management of postoperative micturition is hypotonic bladder and the early development of overdistension. Correct postoperative care with adequate bladder drainage time and PVR controls should avoid retention and overflow of urine [5].

Comparative studies of RAH and NSRH support the current opinion that the nerve-sparing technique is associated with faster postoperative restitution of lower urinary tract function [7, 20]. Similarly, laparoscopic NSRH should be related to shorter catheterization time and a lower rate of voiding dysfunctions compared with laparoscopic radical hysterectomy. In the study by Bogani et al., patients were postoperatively catheterized with an indwelling Foley catheter for a median of 3.5 days (range 2–7 days) after laparoscopic NSRH and 5.5 days (range 4–7 days) after laparoscopic radical hysterectomy [21].

Major bladder function changes are observed 6 to 12 months after cervical cancer surgery and vesical functions are restored after adequate postoperative bladder care [2]. Therefore, our control urodynamic examinations were conducted 12 months after surgery because we were sure that the transitional effects of the surgery on bladder function had already been resolved at that time. This was also confirmed by Roh et al., who compared urodynamic findings before surgery and 1, 3, and 12 months after surgery. All urodynamic parameters in women who underwent NSRH had recovered by 3 months after surgery compared with the group of women who underwent radical hysterectomy and who experienced persistent changes in bladder compliance and residual urine 1 year after the surgery [6]. The low NSRH-induced morbidity of the urinary tract confirmed the study evaluating urodynamic examination 3 weeks after laparoscopic NSRH in 35 patients. Complete recovery of bladder function was revealed after removal of the Foley catheter [22].

The only postoperative change in our study was a slight increase in the maximum cystometric capacity without a prolonged voiding phase. Similar results were described by Maneschi et al. in their small study of 15 patients after NSRH, in which pre- and postoperative urodynamic findings were compared. Reduced detrusor activity was observed during the filling phase, which was confirmed by the significant increase in the maximum cystomanometric capacity, and during the voiding phase, which was confirmed by the significant increase in flow time and the time to maximum flow velocity [23].

Abdominal hysterectomy is considered one of the potential risk factors for the development of stress urinary incontinence, but its role remains controversial [24]. In their extensive study, Milsom et al. claimed that after hysterectomy, women reported symptoms of urinary incontinence more often (21% versus 16%) than those without hysterectomy [25]. Other authors claimed that hysterectomy was, together with age above 40 and vaginal childbirth, a risk factor for the development of stress urinary incontinence [26]. Conversely, Demirci et al. reported that hysterectomy did not cause weakened urethral support and thus did not increase the risk of postoperative stress urinary incontinence [27].

Particularly in young and middle-aged women, urinary incontinence is considered more of a dynamic symptom than a static symptom. Only 40 patients in our study group were postmenopausal (37.7%). Accordingly, we agree with the statement that some women have newly developed symptoms of incontinence after hysterectomy whereas in others, the symptoms of incontinence disappear after surgery [28].

The overall prevalence of urinary incontinence symptoms in our study group before and after surgery was similar to its prevalence in the general adult female population [29]. After surgery, all our premenopausal patients with bilateral salpingo-oophorectomy (it is a part of NSRH at our department and has been performed in all women in the study group) used estrogen replacement therapy. A low prevalence of urinary incontinence symptoms (2.2%) in women after NSRH with a mean age of 44.4 years was recently described by Jiang et al. [11].

Adjuvant radiotherapy was the exclusion criterion for participation in our study because it could significantly affect urinary tract morbidity, and therefore, it could alter the assessment of surgical outcomes regarding quality of life [30].

In terms of strengths, our study met the score for the correct methodology of the study type: it is a prospective study with more than 100 participants and a 1-year postoperative follow-up, and objective preoperative and postoperative urodynamic assessment of lower urinary tract function was performed. Only the 2-day initial introduction of a permanent urinary catheter in our study group of women after laparotomic NSRH is unique. Our study group of 106 patients who underwent NSRH surgery and preoperative and postoperative urodynamic examinations is one of the largest described worldwide.

Our study also had some limitations. Urodynamic studies were performed over a long interval (before and 1 year after surgery), and therefore, we did not record whether any functional urinary tract disorders occurred after surgery and subsequently spontaneously resolved, or did not occur at all. To verify our results, additional similar groups of patients should be analyzed with similar postoperative management of urinary bladder catheterization after NSRH and with objective pre- and postoperative urodynamic assessment. Finally, the absence of a control group was also a limitation of our study.

Conclusion

This study did not show any negative long-term effects of NSRH on bladder function and urinary continence. No postoperative urinary incontinence was observed in women after NSRH. Our study verified the possibility of early permanent urinary catheter extraction on the 2nd postoperative day without impairment of postoperative evacuation function of the urinary bladder.

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Compliance with ethical standards

Conflicts of interest None.

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