

Pelvic Dysfunctions and Quality of Life after Nerve-sparing Radical Hysterectomy: A Multicenter Comparative Study

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Abstract. *Aim: To analyze pelvic dysfunctions, quality of life, and survival after nerve-sparing radical hysterectomy (NSRH) compared to classical radical hysterectomy (RH) for cervical cancer. Patients and Methods: All cervical cancer patients undergoing a RH or a NSRH were evaluated for pelvic dysfunctions and filled in a quality-of-life questionnaire. Results: A total of 56 women were included; 31 underwent RH (group 1) and 25 NSRH (group 2). Postoperatively, a higher number of patients had urinary incontinence ($p=0.02$), urinary retention ($p=0.01$), faecal incontinence ($p=0.01$) and constipation ($p=0.01$) in group 1 versus group 2. Patients referred a higher rate of severe sexual dysfunction after RH compared to NSRH ($p=0.03$). No differences were found in orgasmic frequency and sexual desire; overall quality of life evaluation was more satisfactory after NSRH. Conclusion: NSRH conferred a better clinical outcome with fewer long-term bladder, colorectal and sexual complications. Post-operative quality of life after NSRH was better, with the same overall survival as compared to RH.*

Radical hysterectomy (RH) with systematic pelvic lymphadenectomy is the treatment of choice for women with early-stage or locally advanced cervical cancer, with a 5-year

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survival rate of more than 90%. However, the Wertheim-Meigs RH is associated with long-term morbidities, such as bladder and sexual dysfunctions, and defecation problems, due to damage to the hypogastric and pelvic splanchnic nerves and to the proximal and distal part of the inferior hypogastric plexa (1).

Within the controversial discussion regarding the optimal level of radicality of hysterectomy (2), the concept of nerve-sparing has arisen with the aim of reducing morbidity without compromising the oncological outcome (3-4).

In the 1960's, Kobayashi introduced for the first time the concept of nerve-sparing as a surgical approach for preservation of the pelvic autonomic nerves (5). This concept was then implemented in European Institutions and thereafter developed and described in different techniques, resulting a significant reduction in bladder functions impairment (4-9). Benefits of the nerve-sparing operation technique, compared with non nerve-sparing procedures, have been reported for sexual functioning, bladder and bowel functions (10-14), with promising results with respect to disease-free (DFS) and overall survival (OS). Currently there are no large, prospective, randomized studies comparing nerve-sparing RH (NSRH) with classical RH, thus hindering the widespread use of this technique. The purpose of this retrospective study was therefore to compare classical RH with NSRH with regards to post-operative pelvic dysfunctions, clinical outcome, survival and quality of life.

Patients and Methods

All consecutive patients with early-stage and locally-advanced cervical cancer (FIGO stage IA2-IIIB) who underwent RH or NSRH in the Gynecologic Oncology Unit of the Sacred Heart Hospital of Negrar (Verona) and the Department of Obstetrics and Gynecology of Bologna University Hospital, between January 1997 and November 2009, were enrolled in the study. Data on patient characteristics, tumor

Table I. Clinical profile of 56 patients treated with radical hysterectomy (RH) for cervical cancer (p-values were not significant).

		RH (n=31)	NSRH (n=25)	Total (n=56)
Age, years	Median (SD)	49 (14)	52 (11)	51 (12)
	Range	32-77	30-75	30-77
Histology	SCC	25 (80.6%)	18 (72%)	43 (76.8%)
	AD	6 (19.4%)	7 (28%)	13 (23.2%)
FIGO stage	IA2	3 (9.6%)	3 (12%)	6 (10.7%)
	IB1	12 (38.7%)	11 (44%)	23 (41%)
	IB2	8 (25.8%)	5 (20%)	13 (23.2%)
	IIA	8 (25.8%)	1 (4%)	9 (16%)
	IIB	2 (6.4%)	5 (20%)	7 (12.5%)
Grading	1	3 (9.6%)	2 (8%)	5 (9%)
	2	17 (54.8%)	17 (68%)	34 (60.7%)
	3	11 (35.4%)	6 (24%)	17 (30.3%)
Neoadjuvant chemotherapy		3 (9.6%)	4 (16%)	7 (12.5%)
Adj radiotherapy		11 (35.4%)	5 (20%)	16 (28.5%)
Adj chemoradiotherapy		4 (12.9%)	6 (24%)	10 (17.8%)

RH, Radical hysterectomy; NSRH, nerve-sparing radical hysterectomy; SCC, squamous cervical cancer; AD, adenocarcinoma; Adj: adjuvant.

classification, pathology and surgical factors were analyzed. Tumors were staged according to the guidelines of the International Federation of Gynaecology and Obstetrics. Patients were divided into two groups: patients undergoing a RH were defined as group 1; patients undergoing a NSRH were defined as group 2. Gynecological oncology surgical teams performed all operations. In both Institutions, NSRH and laparoscopic hysterectomies have been carried out since 2003. The criteria of choice for the surgical approach were similar for both surgical teams, according to surgeons' skills and expertise. Regarding the radicality of parametrial resection, the surgical steps of Type III RH, as described by Piver and Rutledge (14) or the current C1 and C2 subtypes of the Querleu-Morrow classification system (16), were followed. Laparoscopic RH was performed according to the technique previously reported by Malzoni *et al.* (17), with technical modifications in parametrial dissection for the nerve-sparing approach, as recently published by our group (18). The follow-up period lasted from the date of surgery until July 2010. All patients underwent pre-operative urodynamic studies to ascertain that bladder functions were not previously affected. Perioperative complications were defined as events occurring within the first 30 days after the operation. Long-term complications were those occurring after postoperative day 30 until the end of follow-up. All patients underwent clinical and instrumental evaluation of bladder functions. The bladder catheter was removed on day 3 followed by self-catheterization after spontaneous voiding, until the detection of normal residual urine, *i.e.* post-voiding residual (PVR) <100 ml on three consecutive assays. Patients performed self-intermittent catheterization at home if they experienced voiding difficulty or urinary retention >100 ml at the time of discharge. The number of days of self-catheterization from discharge until resolution were calculated. Patients not able to void spontaneously after 12 months were considered as "denervated" and submitted to further urodynamic investigations in order to assess the need for sacral neuromodulation. During the follow-up period, at least one year after operation, patients were asked to fill out a questionnaire regarding pelvic function and quality of life. The patients' quality of life was also investigated in a part of the questionnaire concerning subjective

Table II. Intra-operative data.

	RH (n=31)	NSRH (n=25)	Total (n=56)	p-Value
Type of surgery				
LPS	13 (41.9%)	7 (28%)	20 (36%)	0.64
LPT	18 (58%)	18 (72%)	36 (64%)	0.64
Pelvic lymphadenectomy	31 (100%)	25 (100%)	56 (100%)	NA
Para-aortic lymphadenectomy	3 (9.6%)	8 (32%)	11 (19.6%)	0.06
Operative time, min				
Mean (SD)	238 (61)	258 (76)	247 (68)	0.08
Range	180-450	95-420	95-450	
EBL, ml				
Mean (SD)	740 (363)	492 (322)	629 (364)	0.04
Range	50-1400	100-1200	50-1400	
Intraoperative complications				
Vascular lesion	3 (9.6%)	0	3 (5.3%)	
Bowel perforation	1 (3.2%)	0	1 (1.7%)	
Hemorrhage*	9/18 (50%)	2/18 (11.1%)	11/18 (61.1%)	0.01
No. of PN				
Mean (SD)	21(6)	23 (13)	22 (10)	0.06
Range	9-33	9-44	9-44	
No. of PAN				
Mean (SD)	25 (5)	23 (8)	24 (7)	0.08
Range	18-43	15-41	15-43	

LPS, Laparoscopic RH; LPT, abdominal RH; SD, standard deviation; EBL, estimated blood loss; PN, pelvic nodes removed at surgery; PAN, para-aortic nodes removed at surgery; NA, not applicable. *Only patients operated by abdominal approach. Intra-operative hemorrhage was defined as EBL >1000 ml (see text).

perception of their status. The questionnaire was modified from the Bergmark's series (13), and assessed quality of life by a score based on 54 items which take into account sexual function, [according to the Diagnostic and Statistical Manual of Mental Disorders criteria, IV Edition (DSM-IV)] (19) and the psychological status [according to the Short World Health Organization (WHO) Quality of Life (QoL) scores] (20). All patients provided a written informed consent to participate in the questionnaire part of the survey. All patients with impairment in bladder, bowel, rectal and sexual function at the time of answering the questionnaire, and confirmed by a urodynamic test and anorectal manometry, were considered "denervated". DFS was defined as the period from the surgical intervention to cytologically or histologically proven evidence of recurrent disease. OS was defined as the time from date of operation to death from oncological disease. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 17.0 (Chicago, Illinois, USA). GraphPad InStat statistical software, version 3.00, was used to calculate the odds ratios and their corresponding 95% confidence intervals in accordance with the approximation of Woolf. The Fisher's exact test was used to determine the two-sided p-values and statistical significance was assigned at the level of $p < 0.05$. A linear regression model was adopted to calculate the time-trend of considered symptoms. Survival rates were calculated according to the Kaplan-Meier method. The corresponding p-value was computed using the log-rank (Mantel-Cox) test.

Table III. Peri-operative complications (<28 days after operation).

	RH (n=31)	NSRH (n=25)	Total (n=56)	p-Value
Dysuria	8 (25.8%)	0	8 (44.6%)	<0.01
Lymphocele	4 (12.9%)	3 (12%)	7 (12.5%)	0.9
Lymphedema	1 (3.2%)	0	1 (1.7%)	0.8
Lymphorrhea	1 (3.2%)	0	1 (1.7%)	0.8
Fistula	0	2 (8%)	2 (3.4%)	0.7
Incontinence	17 (54.8%)	2 (8%)	19 (33.9%)	<0.01
Urge urinary	9 (29%)	1 (4%)	10 (17.8%)	0.01
Stress urinary	4 (12.9%)	1 (4%)	5 (8.9%)	0.24
Mixed urinary	4 (12.9%)	0	4 (7.1%)	0.06
Use of abdominal torque	8 (25.8%)	1 (4%)	9 (16%)	0.02
Bladder hyposensitivity	8 (25.8%)	1 (4%)	9 (16%)	0.02
Urinary retention	12 (38.7%)	2 (8%)	14 (25%)	<0.01
Self-catheterization at discharge	11 (35.4%)	2 (8%)	13 (23.2%)	0.01
Day of catheter removal >3 days	0	3 (12%)	3 (5.3%)	0.05
Post voiding residual ≥100 ml	6 (19.3%)	0	6 (10.7%)	0.02
Days of self-catheterization				
Mean	529	8.6	408	<0.01
Range	40-1290	4-15	4-1290	
Degree of urinary incontinence at follow-up				
Never/seldom	17 (54.8%)	24 (96%)	41 (73.2%)	<0.01
Sometimes/ Often	14 (45.1%)	1 (4%)	15 (26.7%)	

Results

Fifty-six women were included in the study, out of these 31 underwent RH (group 1) and 25 NSRH (group 2). Patients and tumor stage, type and grading were homogeneous for both groups (Table I). Intra-operative data are listed in Table II. Pelvic lymphadenectomy was performed in all cases, while para-aortic lymphadenectomy was performed in cases in which intra-operative metastatic pelvic nodes were detected. Estimated blood loss (EBL) was significantly higher for group 1 compared to group 2 ($p=0.04$). The intra-operative complication rate was significantly higher in group 1 (38%) than in group 2 (8%) ($p<0.01$), with a total complication rate of 25% (14/56). Patients of group 1 suffered more frequently from dysuria, urinary incontinence and urge incontinence compared with those of group 2. Moreover, in group 1, use of abdominal torque for bladder voiding, bladder hyposensitivity, urinary retention, self-catheterization at discharge and PVR >100 ml were more frequently reported than in group 2 (Table III). These data were reflected in the higher median number of days of self-catheterization after discharge of group 1 patients.

At follow-up examination on post-operative day 30 a higher number of patients in group 1 reported occasional/frequent episodes of urine loss, also verified by urodynamic investigation, with respect to group 2 ($p<0.01$). During the 36-month follow-up, a higher number of patients were affected by urinary incontinence ($p=0.02$), urinary retention ($p=0.01$), fecal incontinence ($p=0.01$) and constipation ($p=0.01$) in group 1

versus group 2 (Figure 1). The linear regression model confirmed a significant difference between the time trend of each pelvic dysfunction during the follow-up period. Patients who experienced long-term complications had undergone postoperative radiotherapy in 50% of the cases, with no difference in frequency between the two groups. All 56 patients of the study completed the questionnaire. The median time of questionnaire administration was 22 months (range 12-38 months). The questionnaire was divided into three sections (Table IV). In analyzing the responses to the questionnaires, no statistical differences were detected between the two groups for urinary incontinence and voiding impairment. None of the differences between the two groups reached statistical significance in terms of bowel-rectal quality of life. Eight patients (25.8%) of group 1 and eight (32%) of group 2 reported not being sexually active in the questionnaire. Psycho-physical distress due to dyspareunia was significantly higher in group 1 *versus* group 2 ($p<0.01$). While the differences in rates of vaginal dryness were not statistically significant, psycho-physical distress due to vaginal dryness was higher in patients of group 1 compared with those of group 2 ($p=0.02$). Even though no differences were found between the two groups in terms of the average number of sexual intercourses/month after RH, patients of group 1 claimed a statistically higher reduction in frequency of intercourse after RH. Patients' self-evaluation of sexual satisfaction was similar for both groups. As compared with surgery alone, adjuvant radiotherapy did not affect sexual outcome and overall self-evaluation of quality of life (data not

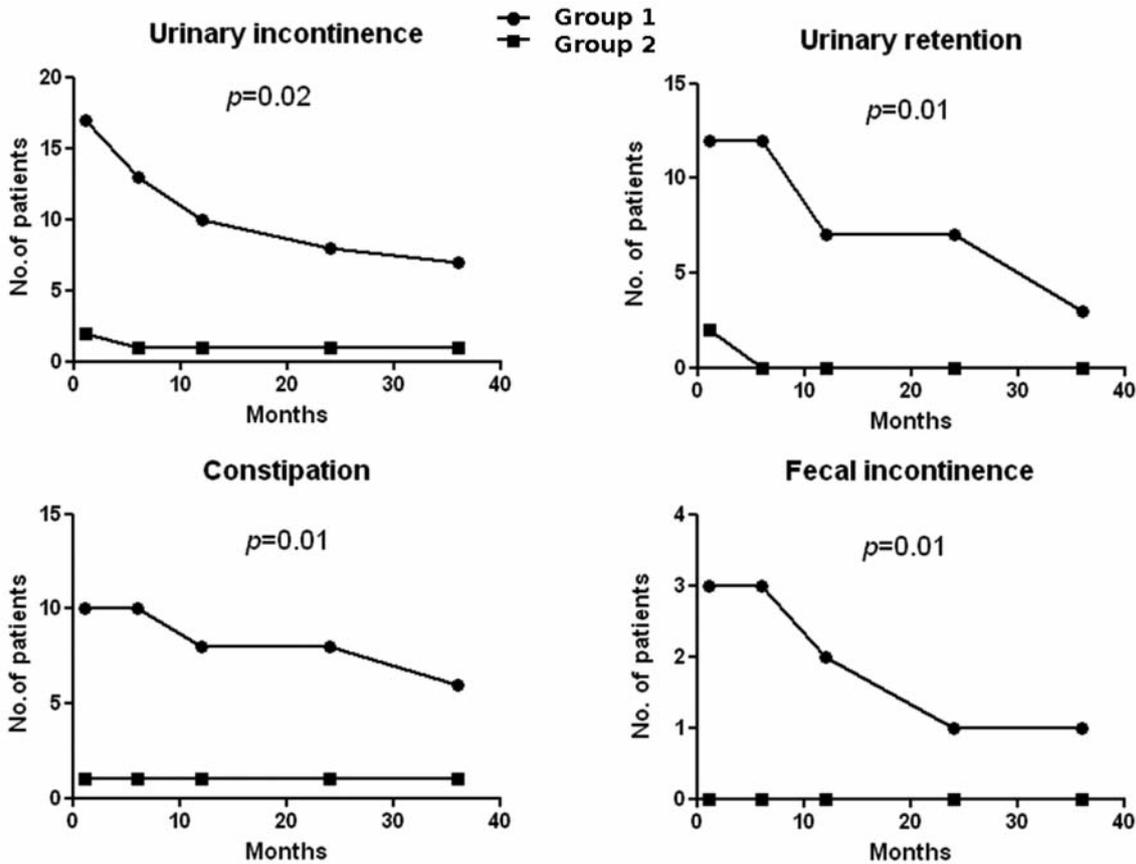


Figure 1. Linear regression model for time-trend of analyzed symptoms in the two study groups.

shown). Detection of severe sexual dysfunction was significantly higher in group 1 as compared to group 2 ($p=0.03$). Finally, post-operative overall quality of life was significantly better in patients of group 2 *versus* those of group 1 ($p=0.03$). After more than 12 months from surgery detection of bladder dysfunctions were significantly different between the two groups; in fact patients of group 1 reported a significantly higher rate of moderate/severe urinary incontinence ($p=0.02$) and retention ($p=0.03$), compared with those of group 2. While moderate/severe constipation was found to be significantly higher for patients of group 1 ($p=0.02$), fecal incontinence rates were statistically comparable between both groups. A sacral pacemaker was indicated if the patient suffered from severe urinary retention and/or incontinence for more than two years. Seven patients from group 1 (22.5%) were defined as being “denervated”, whereas no patient in group 2 was so defined. Three denervated women showed moderate/severe urinary retention and/or incontinence for more than two years, and were theoretically candidates for sacral neuromodulation. However, a pacemaker was implanted in only two cases. The third candidate died from pulmonary recurrence 24 months after intervention. One of the two women

with sacral pacemaker still suffered occasionally from mixed incontinence, but urinary retention and severe constipation were completely solved. The median time of follow-up was 38 (range 12-100) months. DFS was 83.3% for stage IA2, 95.7% for IB1, 100% for IB2, 71.4% for IIA, 71.4% for IIB disease. Cumulative DFS was 89.3%. The median time to relapse was 28 (range 17-44) months for stage IA2, 34 (range 8-93) months for IB1, 39 (range 13-78) months for IB2, 34 (range 14-52) months for IIA and 20 (range 11-46) months for IIB disease. OS was 100% for stage IA2, 95.7% for IB1, 100% for IB2, 71.4% for IIA and 85.7% for IIB disease. Cumulative OS was 92.9% while OS and DFS rates were not significantly different between the groups (Figure 2). Moreover, survival analysis did not show any statistical difference between patients undergoing laparoscopic or abdominal surgery (data not shown).

Discussion

Functional disorders of the lower urinary tract are the most common long-term complications following radical surgery for cancer of the uterine cervix (12). Serious bladder dysfunctions have been reported in up to 70-85% of patients dependent on

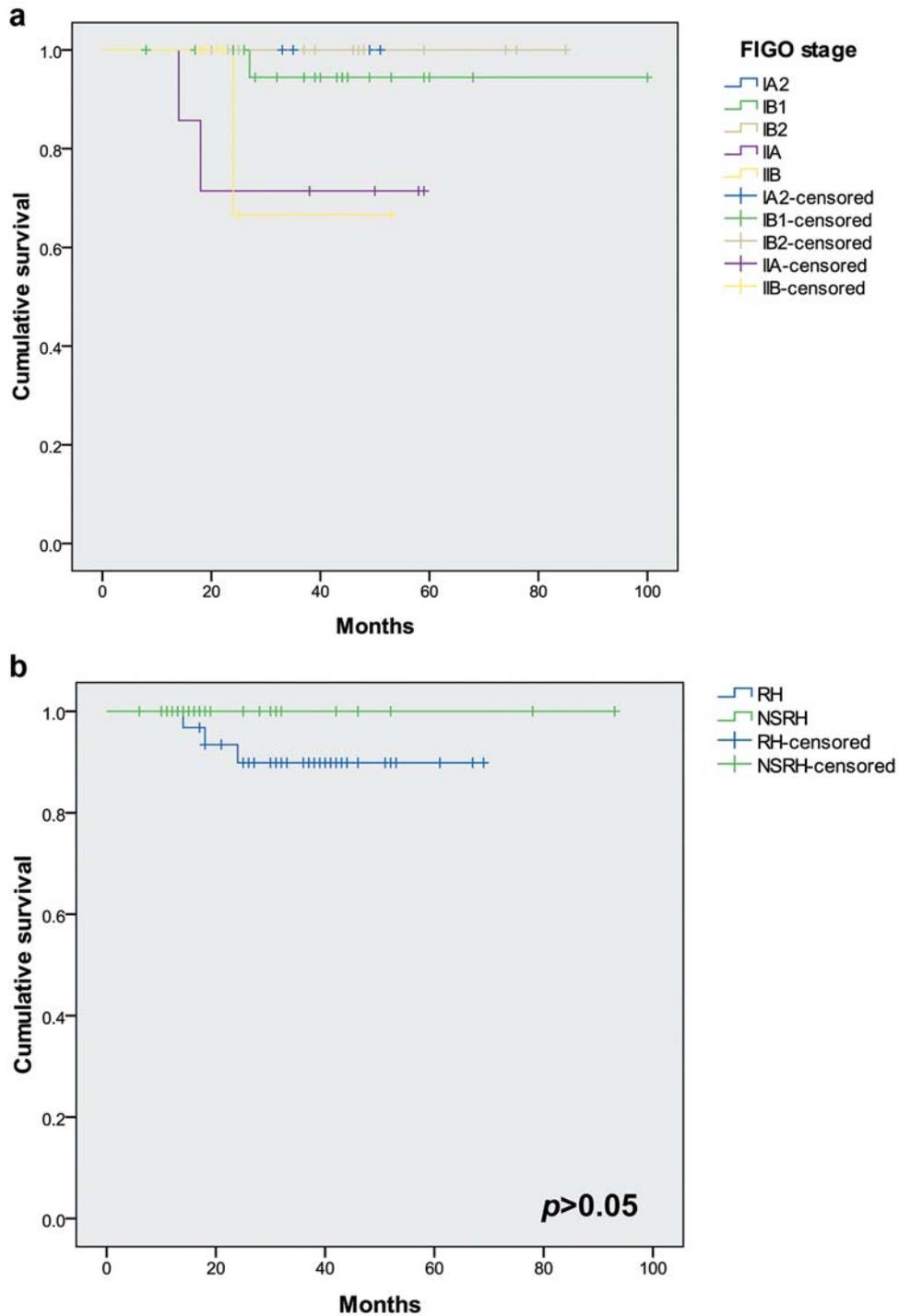


Figure 2. Overall survival of the 56 patients with cervical cancer divided by FIGO stage (a) and type of surgery (b).

how radical the surgery was. Chronic bladder impairment involves emptying difficulties, irritable symptoms of frequency, urgency and urge incontinence, and a reduction of bladder compliance (22). Autonomic neurologic control of the bladder by the parasympathetic system regulates the detrusorial activity

and the orthosympathetic system which is responsible for the tone of internal urethral sphincters. Specific surgical steps of RH may cause risk of nerve injury directly related to the radicality of the operation. In particular, neuroablative lesions of the pelvic plexus, its afferent branches, its efferent bundles at

Table IV. Responses to quality-of-life questionnaire.

		RH (n=31)	NSRH (n=25)	Total (N=56)	p-Value
Urinary incontinence	Never/seldom	31 (100%)	24 (96%)	55 (98.2%)	0.26
	Sometimes	0	1 (4%)	1 (1.7%)	
Difficulty in bladder-emptying	Not at all	29 (93.5%)	25 (100%)	54 (96.4%)	0.19
	A lot	2 (6.4%)	0	2 (3.5%)	
Bowel rectal function	Normal	22 (68.7%)	22 (88%)	44 (78.5%)	0.12
	Constipation	9 (29%)	3 (12%)	12 (21.4%)	
Fecal incontinence	Never	0	0	0	NA
	Seldom	2 (6.4%)	0	2 (3.5%)	
Air incontinence	Never	0	0	0	NA
	Seldom	3 (9.6%)	0	3 (5.3%)	
Able to distinguish air from feces	No	0	0	0	NA
	Not always	2 (6.4%)	0	2 (3.5%)	
Sexual activity	No	8 (25.8%)	8 (32%)	16 (28.5%)	0.61
	Yes	23 (74.1%)	17 (68%)	40 (71.4%)	
No. of sexual intercourses/month	Mean	4	5	9	0.8
	Range	2-6	2-11	2-11	
Change of frequency of sexual intercourse/month	Unchanged	15 (48.3%)	21 (84%)	36 (64.2%)	<0.01
	Reduced	16 (51.6%)	4 (16%)	20 (35.7%)	
Dyspareunia	Not at all/a little	19 (61.2%)	16 (64%)	35 (62.5%)	0.27
	Moderately/a lot/intolerable	4 (12.9%)	1 (4%)	5 (8.9%)	
Distress due to dyspareunia	Not at all/ a little	11 (35.4%)	15 (60%)	26 (46.4%)	<0.01
	Moderately/a lot/Intolerable	12 (38.7%)	2 (6.4%)	14 (25%)	
Vaginal dryness	Not at all/ a little	15 (48.3%)	14 (56%)	29 (51.7%)	0.23
	Moderately/a lot	8 (25.8%)	3 (12%)	11 (19.6%)	
Distress due to vaginal dryness	Not at all	10 (32.2%)	13 (52%)	23 (53.5%)	0.02
	Moderately/a lot/intolerable	13 (41.9%)	4 (16%)	17 (30.3%)	
Use of lubricants	10 (32.2%)	4 (16%)	14 (25%)	0.19	
Sexual desire (libido)	Unchanged	8 (25.8%)	10 (40%)	18 (32.1%)	0.13
	Diminished	15 (48.3%)	7 (28%)	22 (39.2%)	
Vaginal blood loss after sexual intercourse		0	1 (4%)	1 (1.7%)	0.8
Orgasmic frequency	Unchanged	9 (29%)	9 (36%)	18 (32.1%)	0.38
	Diminished	14 (45.1%)	8 (32%)	22 (39.2%)	
Sexual satisfaction	Satisfied	12 (38.7%)	10 (40%)	22 (39.2%)	0.67
	Unsatisfied	11 (35.4%)	7 (28%)	18 (32.1%)	
Postoperative QoL	Unchanged	26 (83.8%)	25 (100%)	51 (91%)	0.03
	Deteriorated	5 (16.1%)	0	5 (8.9%)	
Moderate/severe urinary incontinence >1 year	8 (25.8%)	1 (4%)	9 (16%)	0.02	
Moderate/severe urinary retention >1 year	7 (22.5%)	0	7 (12.5%)	0.03	
Moderate/severe fecal incontinence >1 year	2 (6.4%)	0	2 (3.5%)		
Moderate/severe constipation >1 year	8 (25.8%)	1 (4%)	9 (16%)	0.02	
Severe sexual dysfunction	7 (22.5%)	0	7 (12.5%)	0.03	

NA, Not applicable. *Considered as significant when <0.05.

the time of resection of the uterosacral ligaments, caudad portions of the anterior and posterior parametrium and paravaginal portions of the paracervix may be the principal causes of bladder and/or rectal dysfunctions classically verified after RH (23). This study, although a retrospective analysis, has its strength in the complete homogeneity of the groups for comparison and the use of a questionnaire to carefully evaluate pelvic function and quality of life of these patients. In our series, patients who underwent RH reported a higher rate of urinary incontinence after more than 12 months compared with the NSRH group. Specifically, urge incontinence was

significantly more frequent in group 1, while stress incontinence was equal for both groups. These results showed lesser orthosympathetic damage of the fibers directed to the internal urethral bladder sphincter during NSRH compared to RH. However, for several patients of group 1, bladder continence improved over time, indicating the possibility of restoring the function controlled by the orthosympathetic system. Nevertheless, the number of patients with these symptoms was not statistically comparable between the two groups. As for the detrusorial activity, patients undergoing RH required abdominal pressure to void the bladder more

frequently and reported more significant bladder-hyposensitivity. A significantly higher number of patients of the RH group continued self-catheterization after discharge due to pathological post-voiding residual (PVR>100 ml). After more than 12 months, those in the RH group reported a higher rate of urinary retention compared with those in the NSRH group. This may be due to lesser parasympathetic damage of the parametrial fibers directed to the bladder detrusor muscle during NSRH and, as for several patients of group 1 bladder voiding function improved over time, it is possible that the voiding function controlled by the parasympathetic system can also be restored. Nevertheless, the number of patients with these symptoms was also not statistically comparable between the two groups. Our results show how cases of hypo- and hypertonic bladder are similarly frequent in the late post-operative and in the follow-up period after RH: in fact in our series no great differences between urinary incontinence and urinary retention rates were detected in group 1 compared with group 2. There is little information in literature about anorectal dysfunction after RH. A negative effect of RH on bowel functions was shown reporting on various incidence of severe constipation in 5-10% of the cases (24). Moreover, it is not easy to assess the most common types of bowel dysfunctions. Our results for fecal incontinence were similar in both groups after more than 12 months, even if the linear-regression model analysis showed a significant difference for all the follow-up period (Figure 1). Thus it remains difficult to demonstrate a significant role of RH in anorectal denervation; a larger series is required. The median age at diagnosis for cancer of the *cervix uteri* is 48 years, and more than 54% of cervical cancer patients are younger than 50 years of age, reaching a long survival after the treatments and remaining sexually active (1). After RH, women experience changes in their vaginal anatomy and function, resulting in a final sexual dysfunction. These changes include shortening and inelasticity of the vagina, larger resections of the paracolpium, and loss of ovarian function (25). Moreover, radiotherapy is a contributing factor to sexual dysfunction, in particular dyspareunia and vaginal dryness, further shortening and inelasticity due to fibrosis and vascular reaction of the irradiated tissues. However, in our series, patients underwent adjuvant radiotherapy or chemoradiotherapy in comparable percentages in both groups, thus not representing a confounding factor for the final results and quality of life was not affected in either group compared with surgery alone. The autonomic nerves are responsible for sexual arousability, due to neurogenic control of the blood vessels of the vaginal wall, which regulate vasoconstriction/dilation and the lubrication-swelling response (23). Some authors reported short-term adverse effects on sexual function after RH *i.e.* vaginal dryness, reduced sexual activity, dyspareunia, short vagina and sexual dissatisfaction (25, 26). Moreover, in their cross-sectional study, Bergmark *et al.*, using an anonymous questionnaire on vaginal changes and sexual functions, found

that women after treatment for cervical cancer had lesser lubrication and genital swelling during arousal and a shorter vagina during intercourse with respect to controls (13). Our experience confirms negative effects of RH on sexual function. Differently from Bergmark *et al.*, we compared two groups of patients with cervical cancer undergoing two different surgical techniques of RH. Those who underwent RH reported a higher rate of severe sexual dysfunction compared with the NSRH group. The number of sexually active patients after RH or NSRH was comparable, totalling in 71.4% of the whole population studied. Globally, we found a higher rate of reduction in the number of sexual intercourses after surgery in the RH group compared to the NSRH group. Even though the need for lubricants was similar in both groups, the overall percentage of patients with symptoms (25%) was higher than the one reported by Bergmark *et al.* in the cancer group (16%). Moreover, no statistical differences were found in terms of dyspareunia and vaginal dryness, however, a higher level of distress due to these symptoms was reported by the patients in the RH group. Thus, our study evidenced a lower psychophysical distress associated with vaginal changes and sexual outcome in the NSRH group. No differences were found in orgasmic frequency and sexual desire, indicating that the physical changes induced by cervical cancer and the RH do not impact this aspect of sexuality. Moreover, patients reported a similar level of satisfaction with their partners, suggesting that the overall sexual satisfaction consists of a complexity of aspects including the presence of orgasm, sexual desire and the psychological well-being also related to the consciousness of being alive and free from disease after the follow-up period (27). The patients' overall quality of life evaluation was more satisfactory after NSRH and no patient of this group reported a deterioration in their quality of life ($p=0.03$). In our series NSRH was shown to be a safe treatment for early-stage cervical carcinoma, with OS and DSF rates as high as 88-90%, without significant differences compared to RH. This study demonstrated a better clinical outcome, lesser long-term bladder, colorectal and sexual complications, a better postoperative quality of life and the same survival results for NSRH compared with RH for patients with early-stage and locally advanced cervical carcinoma. The nerve-sparing technique was performed with success in all the patients with an adequate surgical and oncological radicality and with promising results regarding bladder, ano-rectal and sexual function. The results of this study confirm data already published in other series, showing the advantages of this technique when compared to RH, with similar survival rates. Nevertheless, NSRH is not yet a properly standardized technique and many oncological institutions still perform classical RH (1, 11). In anticipation of a prospective randomized controlled trial comparing RH with NSRH with an adequate number of patients and follow-up, future perspectives are addressed towards categorization and definition of the

anato-mo-surgical parametrial nomenclature of the nerve-sparing technique in order to standardize the surgical steps leading to more reproducible results.

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References

- 1 Rob L, Halaska M and Robova H: Nerve-sparing and individually tailored surgery for cervical cancer. *Lancet Oncol* 11: 292-301, 2010.
- 2 Landoni F, Maneo A, Cormio G, Perego P, Milani R, Caruso O and Mangioni C: Class II versus class III radical hysterectomy in stage IB-IIA cervical cancer: a prospective randomized study. *Gynecologic Oncology* 80: 3-12, 2001.
- 3 Okabayashi H: Radical abdominal hysterectomy for cancer of the cervix uteri, modification of the Takayama operation. *Surg Gynecol Obstet* 33: 335-341, 1921.
- 4 Yabuki Y, Asamoto A, Hoshiba T, Nishimoto H, Nishikawa Y and Nakajima T: Radical hysterectomy: an anatomic evaluation of parametrial dissection. *Gynecologic Oncology* 77: 155-163, 2000.
- 5 Kobayashi T: Abdominal radical hysterectomy with pelvic lymphadenectomy for cancer of cervix, Second Edition. Tokyo: Nazando 86: 1961.
- 6 Fujii S: Anatomic identification of nerve-sparing radical hysterectomy: a step-by-step procedure *Gynecologic Oncology* 111: 33-41, 2008.
- 7 Hockel M, Konerding MA and Heussel CP: Liposuction-assisted nerve-sparing extended radical hysterectomy: oncologic rationale, surgical anatomy, and feasibility study. *Am J Obstet Gynecol* 178: 971-976, 1998.
- 8 Possover M, Stober S, Plaul K, Schneider A: Identification and preservation of the motoric innervation of the bladder in radical hysterectomy type III. *Gynecol Oncol* 79: 154-157, 2000.
- 9 Trimbos JB, Maas CP, Deruiter MC, Peters AA and Kenter GG: A nerve sparing radical hysterectomy: guidelines and feasibility in Western patients. *Int J Gynecol Cancer* 11: 180-186, 2001.
- 10 Raspagliesi F, Ditto A, Kusamura S, Fontanelli R, Spatti G, Solima E, Zanaboni F and Carcangiu ML: Nerve-sparing radical hysterectomy: a pilot study. *Tumori* 89(5): 497-501, 2003.
- 11 Maas CP, Trimbos JB, De Ruitter MC, Van de Velde CJ and Kenter GG: Nerve sparing radical hysterectomy: latest developments and historical perspective. *Crit Rev Oncol* 48: 271-279, 2003.
- 12 Zullo MA, Mancini N, Angioli R, Muzii L and Panici PB: Vesical dysfunctions after radical hysterectomy for cervical cancer: a critical review. *Crit Rev Oncol Hematol* 48: 287-293, 2003.
- 13 Bergmark K, Avall-Lundqvist E, Dickman PW, Henningsohn L and Steineck G: Vaginal changes and sexuality in women with a history of cervical cancer. *N Engl J Med* 340: 1383-1389, 1999.
- 14 Piver MS, Rutledge F and Smith JP. Five classes of extended hysterectomy for women with cervical cancer. *Obstet Gynecol* 44: 265-272, 1974.
- 15 Sood AK, Nygaard I, Shahin MS, Sorosky JI, Lutgendorf SK and Rao SS: Anorectal dysfunction after surgical treatment for cervical cancer. *J Am Coll Surg* 195(4): 513-519, 2002.
- 16 Querleu D and Morrow CP: Classification of radical hysterectomy. *Lancet Oncol* 9: 297-303, 2008.
- 17 Malzoni M, Tinelli R, Cosentino F, Fusco A and Malzoni C: Total laparoscopic radical hysterectomy versus abdominal radical hysterectomy with lymphadenectomy in patients with early cervical cancer: our experience. *Ann Surg Oncol* 16(5): 1316-1323, 2009.
- 18 Ceccaroni M, Pontrelli G, Spagnolo E, Scioscia M, Bruni F, Paglia A and Minelli L: Parametrial dissection during laparoscopic nerve-sparing radical hysterectomy: a new approach aims to improve patient's postoperative quality of life. *Am J Obstet Gynecol* 202(3): 320, 2010.
- 19 Diagnostic and Statistical Manual of Mental Disorders, 4th ed., American Psychiatric Association, Washington DC, 2000.
- 20 The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. *Soc Sci Med* 41(10): 1403-1409, 1995.
- 21 Cibula D, Velechovska P, Sláma J, Fischerova D, Pinkavova I, Pavlista D, Dundr P, Hill M, Freitag P and Zikan M: Late morbidity following nerve-sparing radical hysterectomy. *Gynecologic Oncology* 116: 506-511, 2010.
- 22 Butler-Manuel SA, Summerville K, Ford A, Blake P, Riley AJ, Sultan AH, Monga AK, Stanton SL, Shepherd JH and Barton DP: Self-assessment of morbidity following radical hysterectomy for cervical cancer. *J Obstetrics Gynaecol* 19(2): 180-183, 1999.
- 23 Ercoli A, Delmas V, Gadonneix G, Fanfani F, Villet R, Paparella P, Mancuso S and Scambia G: Classical and nerve-sparing radical hysterectomy: an evaluation of the risk of injury to the autonomous pelvic nerve. *Surg Radiol Anat* 25: 200-206, 2003.
- 24 Barnes W, Waggoner S, Delgado G, Maher K, Potkul R, Barter J and Benjamin S: Manometric characterization of rectal dysfunction following radical hysterectomy. *Gynecol Oncol* 42: 116-119, 1991.
- 25 Jensen PT, Groenvold M, Klee MC, Thranov I, Petersen MA and Machin D: Early-stage cervical carcinoma, radical hysterectomy, and sexual function. *Cancer* 100: 97-105, 2004.
- 26 Pieterse QD, Maas CP, ter Kuile MM, Lowik M, van Eijkeren MA, Trimbos JB and Kenter GG: An observational longitudinal study to evaluate miction, defecation, and sexual function after radical hysterectomy with pelvic lymphadenectomy for early-stage cervical cancer. *Int J Gynecol Cancer* 16: 1119-1129, 2006.
- 27 Andersen BL: Predicting sexual and psychologic morbidity and improving the quality of life for women with gynecologic cancer. *Cancer* 71(Suppl): 1678-1690, 1993.

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