Impact of Nerve-Sparing Radical Hysterectomy on Pelvic Dysfunctions and Overall Quality of Life in Cervical Cancer: A Comparative Clinical Study

Original Article

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ABSTRACT

Background and Aims: The study aims to compare pelvic dysfunctions and quality of life in cervical cancer patients following nerve-sparing radical hysterectomy (NSRH) and conventional radical hysterectomy (CRH), and to assess the oncologic safety of NSRH through comparing survival outcomes of both techniques.

Patients and Methods: All patients with stages I and II cervical cancer at the National Cancer Institute, Cairo University who underwent NSRH or CRH from 2016 to 2018 were included in the study and were assessed for pelvic dysfunctions and survival outcomes.

Results: Fifty-two patients were enrolled in the study. A study group (NSRH group) of 25 patients and a control group (CRH group) of 27 patients. All patients signed an informed consent after a detailed account of the procedure, its expected outcome, and complications had been explained to them. The incidence of urine retention, urinary incontinence, severe constipation, and sexual dysfunction was higher among the CRH patients. There was a slight difference in disease-free survival and overall survival in both groups.

Conclusion: The severity of pelvic dysfunctions was less after NSRH. NSRH is an oncologically safe technique as well.

Key Words: cancer cervix, conventional radical hysterectomy, nerve-sparing radical hysterectomy, pelvic autonomic nerve injury, pelvic dysfunctions.

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INTRODUCTION

Radical hysterectomy is the standard treatment for women with cancer of the cervix in the early stages, with a 5-year survival rate reaching around 90%. However, conventional radical hysterectomy (CRH) is accompanied by long-term sequelae, including bladder, sexual, and defecation dysfunction due to the damage to the hypogastric nerves, pelvic splanchnic nerves, the inferior hypogastric plexus itself, or its branches [1]. Despite radical hysterectomy having good survival results, at the cost of bladder dysfunction, colorectal motility disorders, and lymphedema, where autonomic nerve damage during surgery has a fundamental role in the development of these complications [2]. Lower urinary tract dysfunctions are the most common complications after radical hysterectomy^[3]. Bladder functional disorders have been reported in 70-85% of patients [3]. In literature, there is not much information about anorectal dysfunction following radical hysterectomy^[4]. The reported incidence of severe constipation after radical hysterectomy is 5-10%[4]. Drastic changes in the vaginal anatomy and function are encountered in women following radical hysterectomy ending up in final sexual dysfunction [5]. In the 1960s, the

concept of nerve-sparing has appeared as a surgical proposal for pelvic autonomic nerve conservation that resulted in a remarkable cutback in post-RH bladder dysfunction ^[6]. Comparative studies have been published comparing the results of nerve-sparing radical hysterectomy (NSRH) with classical radical hysterectomy regarding bladder, sexual, and bowel dysfunctions, with promising results regarding disease-free survival (DFS) and overall survival (OS) ^[7–9]. The oncologic safety of NSRH for cervical cancer has been tested and NSRH is rendered a safe technique for the management of early-stage cervical cancer with better results regarding postoperative morbidity when compared to classic RH ^[10,11].

PATIENTS AND METHODS

All patients with early and locally advanced-stage cancer of the cervix who underwent RH or NSRH at the National Cancer Institute, Cairo University from January 2016 till December 2018 were included in the study. Data regarding patient characteristics, tumor characteristics, and surgical factors were recorded and analyzed. All patients signed a consent after receiving a detailed account of the procedure, its expected outcome, and adverse events.

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All surgeries were carried out at the Gynecological Oncology Department at the NCI. The extent of radicality of the procedure was followed as defined by Querlow-Morrow's classification system [12]. The technique used for NSRH was that described by Bin et al. [13]. The followup period lasted from the date of surgery till January 2024. Preoperatively, all patients underwent urodynamic studies to exclude preoperative bladder dysfunction, and urinary catheters were removed after 5 days, followed by catheterization if voiding difficulty or postvoiding residual urine volume (PVR) was more than 100 ml. Perioperative complications were defined as those occurring in the first 30 days postoperative. Long-term complications were calculated from 1 to 12 months follow-up. Patients who failed to establish normal voiding after 12 months of follow-up. Patients who failed to establish normal voiding after months were considered denervated. All patients answered the female sexual function index questionnaire for sexual function evaluation. SPSS (Statistical Package, version 28) was used to analyze the data. Frequency and percentage were used to summarize qualitative data. x2 was used to compare qualitative data. From the date of diagnosis until death or the last follow-up date, the OS will be determined. DFSs was calculated from complete remission till the date of documented relapse, death, or last follow-up. The Kaplan-Meier technique was used to conduct the survival analysis. The log-rank test was used to compare two survival curves. A P value less than 0.05 was considered significant.

RESULTS

The initial cohort included 52 patients (27 in the CRH group and 25 in the NSRH group), 29 patients were excluded from the sexual function evaluation (15 in the CRH group and 14 in the NSRH group) either because they were sexually inactive or because of marital issues upon cancer diagnosis or because of postoperative complications/recurrence and there was no room for sexual

evaluation. Sociodemographic and tumor characteristics are listed in (Table 1).

Intraoperative factors are listed in (Table 2). Pelvic lymphadenectomy was carried out in all our patients, while none of our patients had paraaortic lymphadenectomy done. EBL (>500 ml) was significantly higher in the CRH group (100%) and 16% in the NSRH group (P<0.001) while EBL (<500 ml) was higher in the NSRH group (84%) than CRH group (0%) (P<0.001). Operative time was significantly higher in the NSRH group (<240 min, 77.8% in the CRH group and 24% in the NSRH group) (>240 min, 22.2% in the CRH group and 76% in the NSRH group) (P<0.001).

Comparisons between perioperative complications among groups are listed in (Table 3). The incidence of dysuria, urgency, postoperative incontinence, urine retention, and postoperative retention was significantly higher in the CRH group. Regarding sexual function, the incidence of vaginal dryness and dyspareunia was significantly higher in the CRH group (P=0.019 and P<0.001, respectively).

Comparison between pelvic complications after 1-year follow-up is illustrated in (Table 4). During the followup period, the patients showed improvement or recovery from urinary complications, which was higher in the NSRH group. All patients who were evaluated for sexual dysfunction answered the female sexual function index questionnaire. The incidence of severe sexual dysfunction at 1 year was higher in the CRH group but did not reach statistical significance. At 1 year follow-up, the incidence of constipation was much higher in the CRH group (25.9%) than in the NSRH group (4%) (P=0.029). Regarding the DFS, the 5-year DFS for the NSRH group was 84 and 85.2% for the CRH group. For the OS, the 5-year survival rate for the NSRH group was 88%, and 85.2% for the CRH group. The resemblance of the DFS and OS rates between the two groups is in favor of the oncologic safety of the NSRH technique (Figures 1–5).

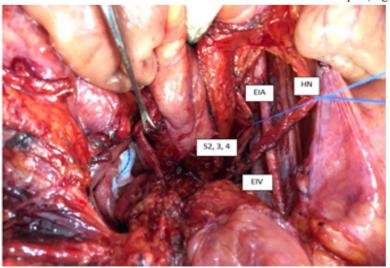


Fig. 1: Preserved right hypogastric nerve, S2, 3, 4 roots, and IHP.

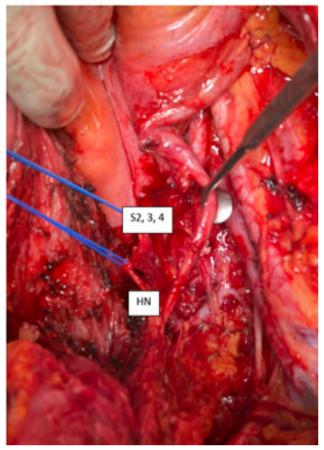


Fig. 2: Preserved left hypogastric nerve, S2, 3, 4 roots, and IHP.

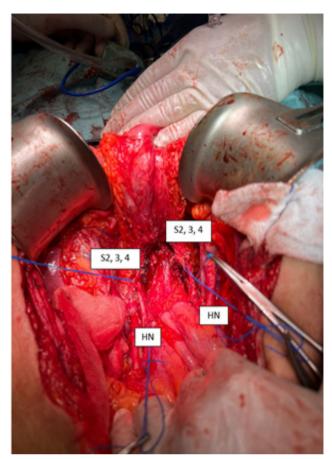
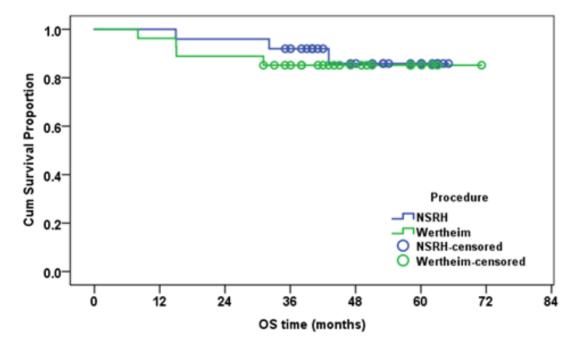


Fig. 3: Preserved hypogastric nerve, S2, 3, 4 roots, and IHP on both sides.



 $\textbf{Fig. 4:} \ Comparison \ between \ cumulative \ disease-free \ survival \ of the \ NSRH \ group \ and \ the \ CRH \ group. \ CRH, \ conventional \ radical \ hysterectomy; \ NSRH, \ nerve-sparing \ radical \ hysterectomy.$

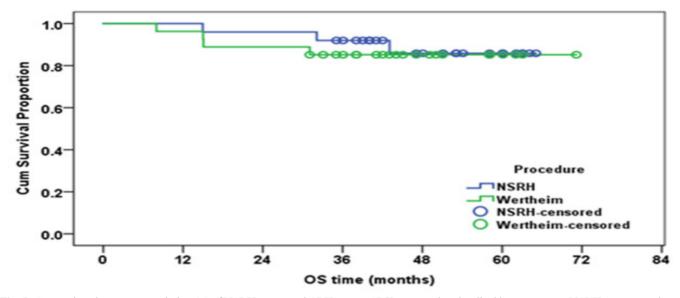


Fig. 5: Comparison between cumulative OS of NSRH group and CRH group. CRH, conventional radical hysterectomy; NSRH, nerve-sparing radical hysterectomy.

Table 1: Sociodemographic and tumor characteristics among the participants.

	Total [n (%)]	NSRH group [n (%)]	Wertheim group [n (%)]	P value
Age (years)				
<50 years	24 (46.2)	12 (48)	12 (44.4)	0.797
≥50 years	28 (53.8)	13 (52)	15 (55.6)	
Figo. stage				
IB1+IB2+IB3	45 (86.5)	22 (88)	23 (85.2)	1.000
IIIC1	7 (13.5)	3 (12)	4 (14.8)	
Histology				
SCC	42 (80.8)	22 (88)	20 (74.1)	0.203
Adenocarcinoma+mixed adenosquamous	10 (19.2)	3 (12)	7 (25.9)	
Grade				
II	25 (48.1)	8 (32)	17 (63)	0.026
III	27 (51.9)	17 (68)	10 (37)	
Lymphovascular invasion				
No	44 (84.6)	22 (88)	22 (81.5)	0.705
Yes	8 (15.4)	3 (12)	5 (18.5)	
Parametrial invasion				
No	49 (94.2)	24 (96)	25 (92.6)	_
Yes	3 (5.8)	1 (4)	2 (7.4)	
Tumour size				
<3 cm	18 (34.6)	10 (40)	8 (29.6)	0.432
≥3 cm	34 (65.4)	15 (60)	19 (70.4)	
Lymph node removed				
<20	26 (50)	15 (60)	11 (40.7)	0.165
≥20	26 (50)	10 (40)	16 (59.3)	
Resected vagina				
<3 cm	21 (40.4)	11 (44)	10 (37)	0.209
≥3 cm	31 (59.6)	14 (56)	17 (63)	

No P value due to small number of cases within subgroups.

Table 2: Comparison of intraoperative factors between groups.

	Total [n (%)]	NSRH group [n (%)]	Wertheim group [n (%)]	P value
Operative time				
<240 min	27 (51.9)	6 (24)	21 (77.8)	< 0.001
≥240 min	25 (48.1)	19 (76)	6 (22.2)	
Blood loss				
≤500 ml	21 (40.4)	21 (84)	0	< 0.001
>500 ml	31 (59.6)	4 (16)	27 (100)	
Hemorrhage				
No	48 (92.3)	23 (92)	25 (92.6)	_
Yes	4 (7.7)	2 (8)	2 (7.4)	

Table 3: Comparison of complications between groups.

	Total [<i>n</i> (%)]	NSRH group $[n (\%)]$	Wertheim group $[n \ (\%)]$	P value
Dysuria	6 (11.5)	0	6 (22.2)	0.023
Urgency	10 (19.2)	2 (8)	8 (29.6)	0.048
Postoperative incontinence	12 (23.1)	2 (8)	10 (37)	0.013
Urine retention	9 (17.3)	1 (4)	8 (29.6)	0.025
Vaginal dryness	10 (43.5)	2 (18.2)	8 (66.7)	0.019
Postoperative retention	10 (19.2)	2 (8)	8 (29.6)	0.048
Sexual satisfaction	12 (52.2)	6 (54.5)	6 (50)	
Diminished libido	13 (56.5)	5 (45.5)	8 (66.7)	0.305
Dyspareunia	10 (43.5)	0	10 (83.3)	< 0.001

Table 4: Comparison of pelvic complications at 1 year.

	Total [n (%)]	NSRH group [n (%)]	Wertheim group $[n \ (\%)]$	P value
Urinary incontinenece>1 year				
No incontinence	40 (76.9)	23(92.0)	17 (63.0)	0.011
Stationary incontinence status	7 (12.5)	0	7(25.9)	
Incontinence but recovered	5(9.6)	2 (8)	3(11.1)	
Urine retension>1 year				
Not retention	42 (80.8)	23 (92)	19 (70.4)	0.030
Stationary retention status	6 (11.5)	0	6 (22.2)	
Retention but recovered	4 (7.7)	2 (8)	2(7.4)	
Constipation>1 year				
No	44 (84.6)	24 (96)	20 (74.1)	0.029
Yes	8 (15.4)	1 (4)	7 (25.9)	
Severe sexual dysfunction>1				
year				
No	11 (47.8)	7 (63.6)	4 (33.3)	0.146
Yes	12 (52.2)	4 (36.4)	8 (66.7)	

DISCUSSION

Following radical hysterectomy for cervical cancer, urinary complications as well as urinary tract functional disorders were ranked the most common long-term sequelae^[1]. According to Ceccaroni et al. ^[1] 70–85% of patients experienced bladder dysfunctions where the extent of radicality was the determinant of these functional disorders, including emptying difficulties, urgency, frequency, and incontinence. During radical hysterectomy, some steps of surgery are responsible for the nerve injury, the most important of which is during resection of the uterosacral ligaments, the caudal portions of the parametrium, and the paravaginal portions of the para-cervix^[1]. Long et al. ^[10] in their systematic review and meta-analysis of 17 articles found that their results kept up with the findings of individual studies that postulate that the NSRH technique is associated with a better outcome regarding urinary dysfunctions. In another study, following NSRH they stated that despite many factors including inflammation, electrical burn damage, local edema, and reduced blood flow might contribute to voiding dysfunction following CRH in the immediate postoperative period but still the most important confounding factor in the development of postoperative bladder dysfunction is pelvic autonomic nerve preservation [14]. In some studies, it was found that hysterectomy when combined with age more than 40 and vaginal delivery becomes a risk factor for stress urinary incontinence [15]. In another study, it was stated that urinary incontinence was a dynamic system rather than a static one, especially in young and middle-aged patients (only 37.7% of the study population were postmenopausal). Some women developed postoperative stress incontinence, while others had symptoms of stress incontinence, and following surgery, it disappeared [15]. However, the voiding function of the urinary bladder improved in many patients of the CRH group. From this, it can be concluded that the voiding function under parasympathetic control can be brought back. Still, the number of patients with these symptoms was not comparable statistically within the two groups [1]. Kim et al. [14] postulated that PAN preservation bilaterally decreased DPC compared to unilateral or failed preservation. Other studies showed the same results, some studies showed equal results upon unilateral or bilateral preservation. DPC was compared upon bilateral, unilateral, and failed preservation following C1 RH in two cohort studies, including this study. The results were interpreted as follows: upon bilateral preservation, restoration of the bladder function occurred within 1 week, upon unilateral preservation, it was restored within 1 month and it took 3 months without preservation throughout C1 RH. Yet, it is worth mentioning that following CRH restoration of the bladder function might take the same time after NSRH without PAN preservation [14]. Muallem and colleagues in their study to evaluate oncologic, surgical, and functional outcomes after NSRH, found that 90% of patients had their bladder functions completely restored in the immediate postoperative period and 97% within the first 2 weeks. They

also found that 38% of patients had to receive adjuvant radiotherapy or radiochemotherapy, and their functional outcome did not show any impairment. They justified this because the patients reached R0 resection and that kept the dose of adjuvant radiotherapy at 45 Gy and did not have to receive a brachytherapy boost [16]. No guidelines have been set up for the preventive measures for postoperative UTIs after RH, despite being quite frequent. Traditionally, after RH permanent and transurethral catheterization has been the used method, but suprapubic catheterization proved to be superior to the former methods. Wells et al. [15] reported that suprapubic catheterization was associated with an eightfold lower frequency of postoperative UTI and earlier restoration of voiding function than in transurethral catheterization. Suprapubic catheterization should be the method of choice in case long-term catheterization is needed because it is better than indwelling urethral catheterization in reducing asymptomatic bacteriuria and the incidence of recatheterization. Lower rates of symptomatic UTIs have been reported after intermittent catheterization compared indwelling urinary catheterization. catheterization is said to be easier to use by the patient and the measurement of postvoiding residual volume is also easier [15].

Pooled data propose that cancer has a dramatic influence on women's sexuality, sexual functions, intimate relationships, and sense of self. The quality of life of patients with gynecological malignancies is greatly influenced by sexuality and intimacy-related issues, especially in patients with cervical cancer [17]. Young patients make lots of efforts to improve their sexual quality of life, while menopausal patients are prone to a worse sexual quality of life than young patients owing to reduction in the ovarian endocrine function and organ atrophy. Older patients were found to have less sexual desire, and age was found to be negatively correlated to the sexual quality of life in cervical cancer patients (P<0.01) [17]. Moreover, nerve density can be affected by low estrogen receptors located within the vaginal wall leading to altered contraction of the vaginal vessels. Following (BSO) parasympathetic nerve density decreases and sympathetic nerves take the upper hand causing a decreased relaxation status of the vaginal venous plexus smooth muscles and decreased vaginal lubrication [17]. Radiotherapy and pelvic lymphadenectomy lead to changes in the anatomy most important of which is decreased vaginal length and vaginal wall elasticity. Contributing factors include peripheral nerve damage and hormonal deficiency because of their impact on vaginal lubrication and genital swelling, the segment lost from the vagina and associated fibrosis leads to vaginal narrowing and distortion [17]. Regarding sexual function, following radical hysterectomy vaginal anatomical and functional changes might result in sexual dysfunction. The responsible changes are vaginal shortening and inelasticity, loss of ovarian endocrine function, and paracolpium resection. Radiotherapy is a major contributing factor as well. In addition, the psychological impact must be taken into consideration [18]. In a study of 229 patients (123 patients underwent NSRH and 106 patients underwent CRH), a validated questionnaire was administered at 12 and 24 months postoperative for both groups. The reported dysfunctions included vaginal distortion, dyspareunia, diminished vaginal lubrication, and overall sexual function dissatisfaction. They found that after 12 and 24 months, follow-up sexual activity increased. From this, they concluded that the surgical modality (NSRH or CRH) used did not have an impact on the sexual dysfunction, that is sexual dysfunction was similar among groups [19].

Kim and colleagues in their meta-analysis to compare CRH versus NSRH found that after NSRH, the incidence of constipation decreased. Sympathetic nerves are responsible for internal anal sphincter stimulation and inhibition of defecation while parasympathetic nerves do the reverse. Particularly, some studies proposed that CRH injury to the PAN disrupts the spinal reflex, leading to dysregulation of the internal sphincter and reduction in rectal sensation. Therefore, they hold up the claim that NSRH decreases functional defecation disorders such as constipation [20].

Long et al. [10] in their systematic review and metaanalysis regarding LDFS found that recurrence rates were similar in the NSRH and CRH after 4 years follow-up in one study and after 2 years follow-up in another study. Ditto and colleagues in their study to evaluate the oncologic effectiveness of NSRH. They found that there was no difference between the NSRH group and the CRH group regarding OS, but the 5-year DFS in CRH was significantly higher compared to NSRH [21]. Sakuragi and colleagues, in their study of the oncologic outcomes following Okabayashi-Kobayashi radical hysterectomy for cervical cancer found that the survival outcome for patients with SCC for early and locally advanced stages was excellent. Their findings hold up with the NCCN guidelines, where NSRH is indicated for stage lB1, lB2, and selected cases of stage lB3 and llA1 [22]. The EORTC-GCG stated in their guide of the quality indicators of CRH for cervical cancer that one of the important indicators is that the recurrence rate should not exceed 15-20%. Therefore, the difference in the recurrence rate between the two treatment modalities should not be more than 5% [23].

CONCLUSION

NSRH is a safe, technically feasible procedure whose preliminary results point to fewer postoperative urinary, sexual, and anorectal dysfunctions when compared to CRH. The preliminary results of DFS and OS in both NSRH and CRH are similar but lack statistical significance due to the relatively small sample size. Increasing the sample size and long-term follow-up is recommended for better validation of results.

CONFLICTS OF INTEREST

None declared.

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