Increased incidence of neurogenic bladder after radical hysterectomy for cervical cancer: A nationwide population-based cohort study

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Abstract

Background: The effect of radical hysterectomy for patients with cervical cancer on voiding function remains controversial. The purpose of this study was to examine the association between radical hysterectomy for patients with cervical cancer and the odds of developing neurogenic bladder by using data from the National Health Insurance Research Database (NHIRD) in Taiwan.

Methods: We identified 17 936 patients who underwent radical hysterectomy for cervical cancer between 2000 and 2013 among inpatients registered in the Longitudinal Health Insurance Database in Taiwan. Of the patients, those diagnosed as having cervical cancer without radical hysterectomy were selected and compared as a matched control group. Patients diagnosed as having cervical cancer before the index date, those with neurogenic bladder dysfunction before tracking, and those aged <20 years were excluded. The hazard ratios (HRs) of neurogenic bladder and other variants of interest were further calculated using a multivariate Cox regression analysis. The cutoff p value of <0.05 was regarded as statistically significant.

Results: The adjusted HR (aHR) of subsequent neurogenic bladder was higher in the hysterectomy group (aHR = 1.205; 95% CI, 1.086-1.440; p = 0.029) than in the control group during the follow-up period. As to the age subgroups, the patients aged 20 to 44 years (aHR = 3.321, p = 0.001) had a significantly increased risk of developing neurogenic bladder after radical hysterectomy as compared with those aged 45 to 64 years (aHR = 1.193, p = 0.012).

Conclusion: Patients with cervical cancer undergoing radical hysterectomy have an increased risk of neurogenic bladder, which may result from nerve denervation caused by the operation. These patients should be informed of the potential risk of voiding dysfunction during discussion of the subsequent management for cervical cancer.

Keywords: Hysterectomy; Neurogenic bladder; Regression analysis

1. INTRODUCTION

Cervical cancer is the fourth common cancer and remains one of the major causes of cancer death among women worldwide.[1] In 2018, an estimated 570 000 women were diagnosed as having cervical cancer worldwide, of whom approximately 311 000 died of the disease.[2] In Taiwan, cervical cancer ranked as the seventh most common cancer in 2017, with an age-adjusted incidence rate of 7.93 per 100 000 women.[3] Public health strategies, including human papillomavirus vaccination, Papanicolaou test screening, and early intervention, lower the incidence and mortality in cervical cancer. Interventions depend on the extent of disease at diagnosis and include radical hysterectomy, chemoradiation, or even a combination of both. As >50% of cervical cancer cases are diagnosed at ages <50 years, quality of life without compromising survival outcomes has been emphasized recently.[2,4]

According to the National Comprehensive Cancer Network guideline (version 1. 2021), radical hysterectomy remains the mainstay treatment of cervical cancer and International Federation of Gynecology and Obstetrics stage IA2, IB1, IB2, and select IB3-IIA1 lesions when fertility preservation is not required.[5] Compared with that of simple extrafascial hysterectomy, the extent of radical hysterectomy includes resection of parts of the cardinal and uterosacral ligaments, and the upper 1 to 2 cm of the vagina.[6] Extensive dissection during radical hysterectomy may further injure the pelvic nerves, vascular supply, and neighboring musculature of the pelvis, resulting in lower urinary tract dysfunction. So far, only few small-scale prospective studies suggested a reduction in long-term functional morbidity by nerve-sparing methods.[7,8]

Owing to the inconsistent findings about the risk of neurogenic bladder after radical hysterectomy in previous studies, we

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conducted this large-scale, nationwide, and population-based study to assess the risk of neurogenic bladder after radial hysterectomy for cervical cancer.

2. METHODS

2.1. Data sources

In this study, we used data from the National Health Insurance Research Database (NHIRD) over a 13-year period to investigate the association between neurogenic bladder and hysterectomy in patients with cervical cancer among inpatients registered in the Longitudinal Health Insurance Database (LHID) in Taiwan (2000-2013). The National Health Insurance Program launched in Taiwan was composed of >99% of all residents per year. The NHIRD uses the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to record diagnoses. All neurogenic bladder diagnoses were made by board-certified urologists or gynecologists, and cervical cancer was diagnosed by gynecologists. Several studies have demonstrated the validity and accuracy of the diagnoses in the NHIRD.

2.2. Study design, participants, and ethics

A retrospective matched-cohort study was conducted. We used the ICD-9-CM coding system to identify diagnoses and related procedures. Cervical cancer was defined as ICD-9-CM code 180. Neurogenic bladder was classified as ICD-9-CM codes 596.4 (atony of the bladder), 596.51 (hypertonicity of the bladder), 596.52 (low bladder compliance), 596.53 (paralysis of the bladder), 596.54 (neurogenic bladder), 596.55 (detrusor sphincter dyssynergia), and 596.59 (other functional disorder of the bladder). We enrolled inpatients in whom cervical cancer was newly diagnosed between 2000 and 2013 in Taiwan. Patients diagnosed as having cervical cancer before the index date, those with neurogenic bladder dysfunction before tracking, and those aged <20 years were excluded.

Hysterectomy procedures were classified as ICD-9-CM procedure codes 68.3 (subtotal abdominal hysterectomy), 68.4 (total abdominal hysterectomy), 68.5 (vaginal hysterectomy), 68.6 (radical abdominal hysterectomy), and 68.7 (radical vaginal hysterectomy), and other relevant subgroups. The following parameters were collected from the inpatient LHID: age, income, urbanization level, location, season, and other comorbidities. The urbanization levels were classified and based on the population size and several indicators. The study protocol was approved by the Institutional Review Board of Tri-Service General Hospital, Taiwan, Republic of China (approval no. TSGH-IRB No. B-110-09).

2.3. Comorbidities

The following comorbidities were further assessed: diabetes mellitus (ICD-9-CM code 250), hypertension (ICD-9-CM codes 401–405), depression (ICD-9-CM codes 296.2, 296.3, 296.82, 300.4, and 311), anxiety (ICD-9-CM code 300, excluding 300.4), renal disease (ICD-9-CM codes 580–589), hyperlipidemia (ICD-9-CM code 272), hyperthyroidism (ICD-9-CM code 242), sepsis (ICD-9-CM codes 038, 003.1, and 036.1), pneumonia (ICD-9-CM codes 480–486), liver disease (ICD-9-CM code 571), injury (ICD-9-CM code 800–999), tumor (ICD-9-CM codes 140–208), and stroke (ICD-9-CM codes 430–437).

2.4. Statistical analyses

Statistical analysis was performed with the SPSS version 20 software (IBM Corp., Armonk, NY). The chi-square and Fisher exact tests were used to analyze categorical variables, while the Student *t* test was used to analyzed continuous variables between the subjects with and without radical hysterectomy. The Kaplan–Meier curve analysis and log-rank test were used to determine the cumulative risk of subsequent neurogenic bladder. The hazard ratios (HRs) of neurogenic bladder and the other parameters of interest were calculated using a multivariate Cox regression analysis. A p value <0.05 was considered statistically significant.

3. RESULTS

Of the 11 019 756 individuals registered in the LHID, 41 651 women with cervical cancer were included in the study. All the study individuals were at least 20 years old and initially diagnosed as having cervical cancer between 2000 and 2013. After application of the exclusion criteria, 1858 subjects were excluded; therefore, 39 793 subjects were selected for the subsequent analysis. Among these patients, 17 936 underwent radical hysterectomy and 17 936 who did not undergo radical hysterectomy were included in the age- and index year-matched control group. During the follow-up period, neurogenic bladder was diagnosed in 1087 subjects, including 592 in the hysterectomy group (3.30%) and 495 in the nonhysterectomy group (2.76%). The study algorithm is presented in Fig. 1.

Table 1 shows that at the beginning of the follow-up period, no significant differences in age and comorbidity were observed between the study subjects and controls. Compared with the control group, the study group included more patients from urbanized, northern, middle, or southern areas in Taiwan ($p < 0.001$).

Table 2 shows that at the end of the follow-up period, 1087 (3.03%) of all the enrolled subjects developed neurogenic bladder, including 592 in the study cohort (3.30%) and 495 in the control cohort (2.76%). The study cohort tended to have an increased risk of developing neurogenic bladder at the end of the follow-up period as compared with the control cohort ($p = 0.003$).

Fig. 2 presents the Kaplan–Meier analysis for the cumulative risk of neurogenic bladder between the study and control cohorts. At the third year of follow-up, the difference became significant (log-rank test, $p < 0.005$).

Table 3 shows the results of the Cox regression analysis of the risk factors relevant to the development of neurogenic bladder. The crude HR was 1.225 (95% CI, 1.097-1.868; $p = 0.038$). After adjustment for age, comorbidity, geographical area of residence, urbanization level of residence, and monthly income, the adjusted HR was 1.205 (95% CI, 1.086-1.440; $p = 0.029$). Compared with the patients aged ≥65 years, those aged 20 to 44 years tended to have an increased risk of developing neurogenic bladder after the adjustment (adjusted HR, 1.469; 95% CI, 1.283-1.793; $p < 0.001$). The patients with diabetes mellitus, hypertension, chronic kidney disease, or the highest urbanization level tended to have an increased risk of developing neurogenic bladder after the adjustment.

The patients were associated with an increased risk of neurogenic bladder in the subgroup analysis stratified by age, income, comorbidity, urbanization level, and level of care as compared with the controls (Table 4). With regard to the different age groups, the patients aged 20 to 44 years (adjusted HR, 3.321; $p = 0.001$) had a significantly increased risk of developing neurogenic bladder after radical hysterectomy as compared with those aged 45 to 64 years (adjusted HR, 1.193; $p = 0.012$); no significant risk of developing neurogenic bladder was observed among the patients aged ≥65 years (adjusted HR, 0.825; 95% CI, 0.643-1.004; $p = 0.298$). Regardless of most comorbidities with the exception hyperthyroidism and liver disease, the patients who underwent radical hysterectomy showed a significantly increased risk of developing neurogenic bladder in

Table 1

Characteristics of the study at baseline

Hysterectomy	Total		With		Without		
Variables	N	%	n	%	n	%	*p*
Total	35 872		17 936	50.00	17 936	50.00	
Age (y) (mean ± SD)	51.77 ± 12.82		51.66 ± 11.82		51.88 ± 13.74		0.104
Age group (y)							0.999
20–44	4514	12.58	2257	12.58	2257	12.58	
45–64	14 624	40.77	7312	40.77	7312	40.77	
≧65	16 734	46.65	8367	46.65	8367	46.65	
Insured premium (NT$)							0.147
<18 000	23 321	65.01	11 573	64.52	11 748	65.50	
18 000–34 999	7904	22.03	4015	22.39	3889	21.68	
≧35 000	4647	12.95	2348	13.09	2299	12.82	
Diabetes mellitus							0.902
Without	32 272	89.96	16 140	89.99	16 132	89.94	
With	3600	10.04	1796	10.01	1804	10.06	
Hypertension							0.290
Without	31 433	87.63	15 750	87.81	15 683	87.44	
With	4439	12.37	2186	12.19	2253	12.56	
Depression							0.704
Without	35 698	99.51	17 846	99.50	17 852	99.53	
With	174	0.49	90	0.50	84	0.47	
Anxiety							0.232
Without	35 771	99.72	17 879	99.68	17 892	99.75	
With	101	0.28	57	0.32	44	0.25	
Renal disease							0.943
Without	34 038	94.89	17 021	94.90	17 017	94.88	
With	1834	5.11	915	5.10	919	5.12	
Hyperlipidemia							0.120
Without	35 612	99.28	17 793	99.20	17 819	99.35	
With	260	0.72	143	0.80	117	0.65	
Hyperthyroidism							0.212
Without	35 794	99.78	17 903	99.82	17 891	99.75	
With	78	0.22	33	0.18	45	0.25	
Sepsis							0.512
Without	34 709	96.76	17 343	96.69	17 366	96.82	
With	1163	3.24	593	3.31	570	3.18	
Pneumonia							0.734
Without	35 154	98.00	17 572	97.97	17 582	98.03	
With	718	2.00	364	2.03	354	1.97	
Liver disease							0.177
Without	34 191	95.31	17 068	95.16	17 123	95.47	
With	1681	4.69	868	4.84	813	4.53	
Injury							0.590
Without	34 433	95.99	17 206	95.93	17 227	96.05	
With	1439	4.01	730	4.07	709	3.95	
Tumor							0.154
Without	31 769	88.56	15 841	88.32	15 928	88.80	
With	4103	11.44	2095	11.68	2008	11.20	
Stroke							0.143
Without	35 357	98.56	17 662	98.47	17 695	98.66	
With	515	1.44	274	1.53	241	1.34	
Location							<0.001*
Northern Taiwan	16 370	45.63	8265	46.08	8105	45.19	
Middle Taiwan	8788	24.50	4407	24.57	4381	24.43	
Southern Taiwan	9453	26.35	4875	27.18	4578	25.52	
Eastern Taiwan	1201	3.35	377	2.10	824	4.59	
Outlying islands	60	0.17	12	0.07	48	0.27	
Urbanization level							<0.001*
1 (The highest)	16 610	46.30	8223	45.85	8387	46.76	
2	15 765	43.95	8406	46.87	7359	41.03	
3	928	2.59	390	2.17	538	3.00	
4 (The lowest)	2569	7.16	917	5.11	1652	9.21	

p value (categorical variables: Chi-squared test/Fisher exact test; continuous variables: *t* test).
NT$ = New Taiwan dollar.
*$p < 0.05$.

comparison with those who did not undergo radical hysterectomy (adjusted HR, 1.158-2.871).

4. DISCUSSION

The effects due to radical hysterectomy are divided into early changes in bladder function and long-term voiding dysfunction or neurogenic bladder. The incidence of neurogenic bladder after radical hysterectomy varied widely in previous studies.[9] In 2009, Brooks et al[9] claimed that radical hysterectomy compared with simple extrafascial hysterectomy showed no significant difference in terms of long-term bladder dysfunction. The discrepancy among the studies may be attributed to the variable evaluation methods, definitions of neurogenic bladder, surgical procedures, follow-up intervals, and unstandardized urodynamic parameters. The potential etiology of neurogenic bladder is due to disruption of autonomic fibers innervating the lower urinary tracts during dissection of the parametrium and uterosacral ligaments. Our study demonstrated that the incidence rate of de novo neurogenic bladder after radical hysterectomy for cervical cancer was 3.30%, higher than that in patients treated without radical hysterectomy (2.75%). Even after the adjustment for comorbidities and other covariates, the overall adjusted HR was 1.205 (95% CI, 1.086-1.440; $p = 0.029$); in other words, the patients who underwent radical hysterectomy for cervical cancer had an approximately 1.2-fold increased risk of developing neurogenic bladder.

In the present study, the incidence rate of neurogenic bladder after radical hysterectomy was found to be significantly higher among the patients aged 20 to 44 years than among those aged 45 to 64 and ≥65 years. This indicates that younger individuals are more susceptible to lower urinary tract symptoms caused by the procedure. One possible explanation for the result is that the baseline voiding condition of the elderly are relatively inferior to that of the young population[4]; hence, the deterioration of lower urinary tract symptoms after the surgery is less obvious in the elderly. A possible unrecognized etiology to explain the phenomena among different age groups may exist.

Recent studies have hypothesized that nerve-sparing radical hysterectomy may achieve adequate radicality for an optimal survival benefit for cervical cancer without compromising the postoperative functional outcome of the lower urinary tract and quality of life.[4,10–13] The current findings demonstrated that the adverse effects on voiding function depend on the extent of hysterectomy and nerve-sparing procedure. However, the nerve-sparing technique should be tailored depending on the tumor size, histology, and extent of tumor invasion; otherwise, it may cause a concern of inadequate radicality.[13] The lack of long-term survival evidence, heterogeneity of nerve-sparing techniques, and patient selection bias were the major limitations of the previous studies, which warrant further study with large-scale randomized prospective research designs.

We analyzed the types of bladder dysfunction after radical hysterectomy through assessments using NHIRD data with ICD-9 coding. However, most bladder dysfunctions were classified as 596.54 (neurogenic bladder) or 596.59 (other functional disorders of the bladder), which could not reveal the specific type of bladder dysfunction after radical hysterectomy. Previous studies reported that urodynamic changes after radical hysterectomy included hyposensitivity of the bladder, reduced bladder compliance, detrusor overactivity, increased post-void residue, and reduced maximal urethral closure pressure.[6,14,15] Plotti et al[16] demonstrated that the general incidence of urodynamic voiding dysfunction is approximately 72% according to the included studies. The incidence of decreased bladder compliance was approximately 35% in the studies with follow-up durations >12 months. The incidence rates of detrusor dysfunctions, mixed

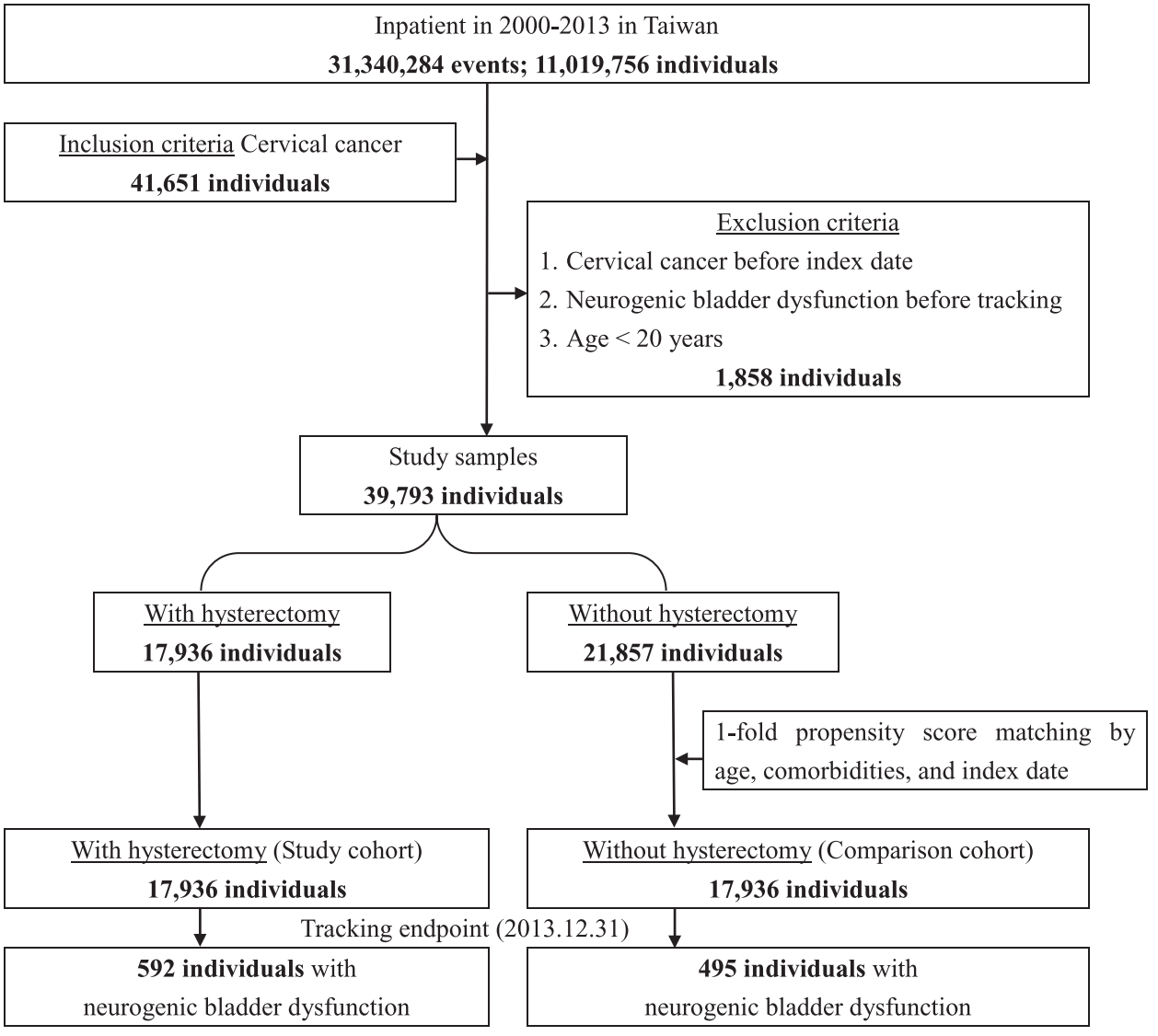


Fig. 1 The flowchart of study sample selection from the National Health Insurance Research Database in Taiwan. Cervical cancer: ICD-9-CM 180. Neurogenic bladder dysfunction: ICD-9-CM 596.4–596.5 (Supplementary Table S1, http://links.lww.com/JCMA/A91). Hysterectomy: ICD-9-CM OP68.3–OP68.7 (Supplementary Table S1, http://links.lww.com/JCMA/A91). Comorbidities are shown in Supplementary Table S1, http://links.lww.com/JCMA/A91. ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification.

Table 2

Characteristics of the study at endpoint

Hysterectomy	Total		With		Without		
Variables	N	%	n	%	n	%	*p*
Total	35 872		17 936	50.00	17 936	50.00	
Neurogenic bladder dysfunction							0.003*
Without	34 785	96.97	17 344	96.70	17 441	97.24	
With	1087	3.03	592	3.30	495	2.76	
Neurogenic bladder dysfunction subgroup							0.018*
Without	34 785	96.97	17 344	96.70	17 441	97.24	
Atony of bladder	186	0.52	101	0.56	85	0.47	
OAB	8	0.02	2	0.01	6	0.03	
Low bladder compliance	5	0.01	4	0.02	1	0.01	
Paralysis of bladder	0	0.00	0	0.00	0	0.00	
Neurogenic bladder, NOS	506	1.41	272	1.52	234	1.30	
Detrusor sphincter dyssynergia	0	0.00	0	0.00	0	0.00	
Other functional disorder of bladder	382	1.06	213	1.19	169	0.94	

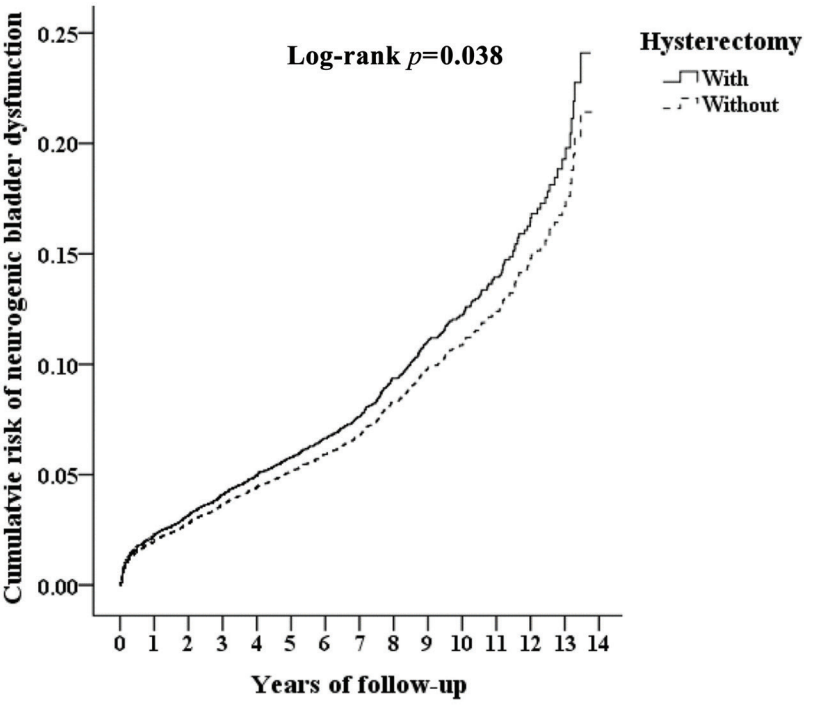
(*Continued next page*)

Table 2 (Continued)

Characteristics of the study at endpoint

Hysterectomy	Total		With		Without		
Variables	N	%	n	%	n	%	*p*
Age (y) (mean ± SD)	62.67±13.19		62.77±14.98		62.57±11.11		0.151
Age group (y)							0.673
20–44	3745	10.44	1848	10.30	1897	10.58	
45–64	13 398	37.35	6697	37.34	6701	37.36	
≧65	18 729	52.21	9391	52.36	9338	52.06	
Insured premium (NT$)							0.147
<18 000	23 321	65.01	11 573	64.52	11 748	65.50	
18 000–34 999	7904	22.03	4015	22.39	3889	21.68	
≧35 000	4647	12.95	2348	13.09	2299	12.82	
Diabetes mellitus							<0.001*
Without	31 277	87.19	15 521	86.54	15 756	87.85	
With	4595	12.81	2415	13.46	2180	12.15	
Hypertension							0.241
Without	31 160	86.86	15 618	87.08	15 542	86.65	
With	4712	13.14	2318	12.92	2394	13.35	
Depression							0.287
Without	35 672	99.44	17 828	99.40	17 844	99.49	
With	200	0.56	108	0.60	92	0.51	
Anxiety							<0.001*
Without	35 673	99.45	17 792	99.20	17 881	99.69	
With	199	0.55	144	0.80	55	0.31	
Renal disease							0.004*
Without	32 467	90.51	16 314	90.96	16 153	90.06	
With	3405	9.49	1622	9.04	1783	9.94	
Hyperlipidemia							0.047*
Without	35 541	99.08	17 752	98.97	17 789	99.18	
With	331	0.92	184	1.03	147	0.82	
Hyperthyroidism							0.299
Without	35 779	99.74	17 884	99.71	17 895	99.77	
With	93	0.26	52	0.29	41	0.23	
Sepsis							0.999
Without	33 524	93.45	16 762	93.45	16 762	93.45	
With	2348	6.55	1174	6.55	1174	6.55	
Pneumonia							0.639
Without	33 737	94.05	16 858	93.99	16 879	94.11	
With	2135	5.95	1078	6.01	1057	5.89	
Liver disease							0.190
Without	35 058	97.73	17 548	97.84	17 510	97.62	
With	814	2.27	388	2.16	426	2.38	
Injury							0.001*
Without	33 391	93.08	16 616	92.64	16 775	93.53	
With	2481	6.92	1320	7.36	1161	6.47	
Tumor							<0.001*
Without	31 209	87.00	15 431	86.03	15 778	87.97	
With	4663	13.00	2505	13.97	2158	12.03	
Stroke							0.342
Without	35 044	97.69	17 508	97.61	17 536	97.77	
With	828	2.31	428	2.39	400	2.23	
Location							<0.001*
Northern Taiwan	15 457	43.09	7741	43.16	7716	43.02	
Middle Taiwan	9449	26.34	4735	26.40	4714	26.28	
Southern Taiwan	9347	26.06	4842	27.00	4505	25.12	
Eastern Taiwan	1515	4.22	585	3.26	930	5.19	
Outlying islands	104	0.29	33	0.18	71	0.40	
Urbanization level							<0.001*
1 (the highest)	14 628	40.78	7239	40.36	7389	41.20	
2	15 989	44.57	8302	46.29	7687	42.86	
3	1441	4.02	675	3.76	766	4.27	
4 (the lowest)	3814	10.63	1720	9.59	2094	11.67	

p value (categorical variables: Chi-squared test/Fisher exact test; continuous variables: *t* test).
NOS = not otherwise specified; NT$ = New Taiwan dollar; OAB = overactive bladder.
*$p < 0.05$.



Hysterectomy	**With** (N=17,936)	**Without** (N=17,936)	*p*
In the tracking of x year(s)	Numbers of neurogenic bladder dysfunction		
1	281	180	0.055
2	336	235	0.051
3	379	293	**0.048***
4	416	332	**0.044***
5	442	362	**0.042***
6	471	384	**0.039***
7	496	404	**0.035***
8	527	438	**0.033***
9	548	459	**0.034***
10	564	466	**0.028***
11	573	479	**0.028***
12	582	489	**0.025***
13	587	493	**0.047***
14	592	495	**0.038***

* $p < 0.05$

Fig. 2 Kaplan–Meier analysis for the cumulative risk of neurogenic bladder dysfunction among patients with cervical cancer aged 20 y and over stratified by hysterectomy with log-rank test.

urinary incontinence, and stress urinary incontinence were 35%, 17%, and 38% at >12 months of follow-up, respectively. The loss of sympathetic innervation may enforce parasympathetic transmission to the bladder detrusor muscle and relax the bladder neck and proximal urethra during the storage phase, which explains the higher incidence rates of detrusor overactivity and stress urinary incontinence after radical hysterectomy.[11] Stress urinary incontinence could be also attributed to a considerable risk of low maximal urethral closure pressure, which may be caused by the denervation of the pelvic plexus and pudendal nerves without preservation of the periurethral tone.[6,11] A urodynamic study may facilitate evaluation and further management of de novo lower urinary tract dysfunction by clinicians after radical hysterectomy.

This study had some limitations. First, the potential effect of adjuvant therapies, including chemotherapy or radiotherapy, cannot be excluded. Second, the ICD-9 coding does not indicate the surgical approach such as open or minimally invasive method,[17,18] extent of radical hysterectomy,[19] use of a nerve-sparing procedure,[4] and stage and histology of cervical cancer. Third, the parity and gravidity of the patients were not described in the covariates of the study. Fourth, the impact on quality of life[20] and severity of voiding dysfunction could not be evaluated. Finally, the true incidence of neurogenic bladder may be underestimated owing to underreported symptoms or diagnoses, which depends on whether patients seek medical care or not.

Patients with cervical cancer undergoing radical hysterectomy have an increased risk of neurogenic bladder, which

Table 3

Factors of neurogenic bladder dysfunction using Cox regression

Variables	Crude HR	95% CI	*p*	Adjusted HR	95% CI	*p*
Hysterectomy						
Without	Reference			Reference		
With	1.225	1.097-1.868	0.038*	1.205	1.086-1.440	0.029*
Age group (y)						
20–44	1.912	1.583-2.311	<0.001*	1.469	1.283-1.793	<0.001*
45–64	1.354	1.191-1.540	<0.001*	1.105	0.965-1.268	0.149
≧65	Reference			Reference		
Insured premium (NT$)						
<18 000	Reference			Reference		
18 000–34 999	0.850	0.385-1.959	0.164	0.971	0.269-4.337	0.267
≧35 000	0.000	-	0.878	0.000	-	0.413
Diabetes mellitus						
Without	Reference			Reference		
With	1.186	1.013-1.390	0.034*	1.563	1.325-1.844	<0.001*
Hypertension						
Without	Reference			Reference		
With	1.858	1.487-1.703	<0.001*	1.572	1.471-1.694	0.003*
Depression						
Without	Reference			Reference		
With	1.162	0.603-2.240	0.653	1.172	0.607-2.266	0.636
Anxiety						
Without	Reference			Reference		
With	1.812	0.862-3.809	0.117	1.792	0.849-3.781	0.126
Renal disease						
Without	Reference			Reference		
With	1.797	1.424-2.017	0.006*	1.182	1.088-1.311	0.022*
Hyperlipidemia						
Without	Reference			Reference		
With	1.119	0.275-2.561	0.390	1.206	0.688-2.554	0.322
Hyperthyroidism						
Without	Reference			Reference		
With	0.000	-	0.908	0.000	-	0.842
Sepsis						
Without	Reference			Reference		
With	1.206	1.006-1.537	0.046*	1.411	0.931-2.551	0.687
Pneumonia						
Without	Reference			Reference		
With	1.173	0.900-1.730	0.421	1.206	0.906-2.356	0.873
Liver disease						
Without	Reference			Reference		
With	0.507	0.299-0.860	0.012*	0.612	0.306-1.084	0.061
Injury						
Without	Reference			Reference		
With	1.613	0.484-2.777	0.646	1.568	0.447-2.723	0.703
Tumor						
Without	Reference			Reference		
With	1.217	1.075-1.377	0.002*	1.526	1.199-2.170	<0.001*
Stroke						
Without	Reference			Reference		
With	1.056	0.438-1.983	0.073	1.019	0.544-2.233	0.336
Location						
Northern Taiwan	Reference			Multicollinearity with urbanization level		
Middle Taiwan	0.838	0.719-1.077	0.064	Multicollinearity with urbanization level		
Southern Taiwan	0.828	0.797-1.080	0.336	Multicollinearity with urbanization level		
Eastern Taiwan	1.894	1.539-2.331	<0.001*	Multicollinearity with urbanization level		
Outlying islands	0.914	0.378-2.206	0.841	Multicollinearity with urbanization level		
Urbanization level						
1 (the highest)	2.016	1.628-2.497	<0.001*	1.810	1.425-2.298	<0.001*
2	1.420	1.030-1.958	0.032*	1.363	0.981-1.868	0.066
3	1.357	1.094-1.684	0.005*	1.231	0.980-1.547	0.075
4 (the lowest)	Reference			Reference		

Adjusted HR: adjusted variables listed in the table.
HR = hazard ratio; NT$ = New Taiwan dollar.
*$p < 0.05$.

Table 4

Factors of neurogenic bladder dysfunction stratified by variables listed in the table using Cox regression

Hysterectomy (with vs without)	With			Without						
Stratified	Event	PYs	Rate (per 10^5 PYs)	Event	PYs	Rate (per 10^5 PYs)	Ratio	Adjusted HR	95% CI	*p*
Total	592	199 290.03	297.05	495	173 546.15	285.23	1.041	1.205	1.086-1.440	0.029*
Age group (y)										
20–44	112	20 396.62	549.11	36	18 819.14	191.29	2.870	3.321	2.993-4.142	0.001*
45–64	325	97 608.57	332.96	263	81 472.44	322.81	1.031	1.193	1.076-1.297	0.012*
≧65	155	81 284.84	190.69	196	73 254.57	267.56	0.713	0.825	0.643-1.004	0.298
Insured premium (NT$)										
<18 000	580	195 170.91	297.18	485	171 213.06	283.27	1.049	1.214	1.094-1.686	0.042*
18 000–34 999	12	3614.41	332.00	10	2193.26	455.94	0.728	1.011	0.759-1.097	0.385
≧35 000	0	504.71	0.00	0	139.83	0.00	-	-	-	-
DM										
Without	499	169 225.64	294.87	402	141 839.87	283.42	1.040	1.194	1.045-1.226	0.002*
With	93	30 064.39	309.34	93	31 706.28	293.32	1.055	1.220	1.118-1.598	0.001*
HTN										
Without	530	160 422.49	330.38	423	128 202.91	329.95	1.001	1.159	1.004-1.196	0.001*
With	62	38 867.54	159.52	72	45 343.24	158.79	1.005	1.264	1.148-1.500	0.001*
Depression										
Without	577	197 629.26	291.96	491	172 447.29	284.72	1.025	1.186	1.069-1.225	0.004*
With	15	1660.77	903.20	4	1098.86	364.01	2.481	2.871	2.487-3.016	<0.001*
Anxiety										
Without	588	198 562.53	296.13	492	172 898.88	284.56	1.041	1.204	1.085-1.338	0.008*
With	4	727.50	549.83	3	647.27	463.49	1.186	1.373	1.237-1.599	<0.001*
Renal disease										
Without	559	188 448.07	296.63	459	155 486.42	295.20	1.005	1.163	1.048-1.200	0.022*
With	33	10 841.96	304.37	36	18 059.73	199.34	1.527	1.367	1.292-1.671	0.014*
Hyperlipidemia										
Without	582	194 558.61	299.14	492	170 859.17	287.96	1.039	1.202	1.083-1.137	0.035*
With	10	4731.42	211.35	3	2686.98	111.65	1.893	2.190	1.874-2.227	<0.001*
Hyperthyroidism										
Without	592	198 541.01	298.18	495	172 917.27	286.26	1.042	1.205	1.086-1.440	0.029*
With	0	749.02	0.00	0	628.88	0.00	-	-	-	-
Sepsis										
Without	566	182 796.35	309.63	470	151 888.07	309.44	1.001	1.158	1.042-1.384	0.026*
With	26	16 493.68	157.64	25	21 658.08	115.43	1.366	1.580	1.424-1.987	0.008*
Pneumonia										
Without	584	188 185.46	310.33	490	159 679.10	306.87	1.011	1.170	1.055-1.107	0.039*
With	8	11 104.57	72.04	5	13 867.05	36.06	1.998	2.321	2.083-2.897	0.011*
Liver disease										
Without	587	195 175.25	300.76	486	168 076.44	289.15	1.040	1.207	1.096-1.508	0.022*
With	5	4114.78	121.51	9	5469.71	164.54	0.738	0.854	0.670-1.021	0.542
Injury										
Without	552	174 569.04	316.21	461	146 315.98	315.07	1.004	1.161	1.047-1.388	0.034*
With	40	24 720.99	161.81	34	27 230.17	124.86	1.296	1.499	1.351-1.792	0.001*
Tumor										
Without	308	131 720.93	233.83	241	103 327.45	233.24	1.003	1.160	1.045-1.386	0.033*
With	284	67 569.10	420.31	254	70 218.70	361.73	1.162	1.344	1.211-1.609	0.011*
Stroke										
Without	570	191 590.21	297.51	480	168 048.00	285.63	1.042	1.205	1.086-1.341	0.025*
With	22	7699.82	285.72	15	5498.15	272.82	1.047	1.212	1.092-1.508	0.039*
Urbanization level										
1 (the highest)	287	62 678.15	457.89	198	60 597.55	326.75	1.401	1.621	1.461-1.963	<0.001*
2	226	93 985.21	240.46	215	77 387.23	277.82	0.866	1.001	0.903-1.197	0.065
3	27	12 428.45	217.24	32	12 542.01	255.14	0.851	0.982	0.888-1.114	0.104
4 (the lowest)	52	30 198.22	172.20	50	23 019.36	217.21	0.793	0.917	0.824-1.096	0.227

Adjusted HR: adjusted for the variables listed in Table 3.

DM = diabetes mellitus; HR = hazard ratio; HTN = hypertension; NT$ = New Taiwan dollar; PYs = person-years.

*$p < 0.05$.

may be caused by the disruption of the autonomic nerve fibers during the procedure. These patients should be informed about the potential risks of lower urinary tract dysfunction during discussion of the subsequent management for cervical cancer.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://doi.org/10.1097/JCMA.0000000000000264.

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