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Urinary retention between nerve-sparing radical hysterectomy and radical hysterectomy for cervical cancer

A meta-analysis

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Abstract

This study intended to assess the urinary retention between nerve-sparing radical hysterectomy and radical hysterectomy in cervical cancer. Relevant studies were selected from databases of PubMed, Embase, Wanfang, and China National Knowledge Internet with the last report up to January 15, 2022. Hazard ratio (HR) and 95% confidence interval (CI) were chosen as the evaluation index. Heterogeneity was assessed using Cochran *Q* test and I^2 test. Subgroup analysis was conducted based on areas and cancer types (primary and metastatic cancer). A total of 8 articles (retrospective cohort studies) were selected in the meta-analysis. There were significant correlations between nerve-sparing radical hysterectomy and radical hysterectomy in related with urinary retention (HR [95% CI] = 1.78 [1.37, 2.31], $P < .001$) and (HR [95% CI] = 2.49 [1.43, 4.33], $P = .001$) of cervical cancer patients. Egger test revealed a significant publication bias ($P = .014$). Sensitivity analysis via omitting 1 study at each time showed that omission of any study made significant difference ($P < .05$), indicating reliability and good stability for the analysis. Additionally, there were significant heterogeneities in most subgroups.

Abbreviations: CI = confidence interval, HR = hazard ratio, RCT = randomized controlled trial.

Keywords: cervical cancer, meta-analysis, prognosis, urinary retention

1. Introduction

Cervical cancer is the most common gynecologic malignant tumor, extensive panhysterectomy is a radical surgery for the treatment of cervical cancer.[1,2] The wide range of surgical resections (including the uterus, fallopian tube, the upper part of the vagina, the main ligament, and the paracolpium) and the complete dissection of the pelvic lymph nodes often brings a number of postoperative complications such as bladder dysfunction (anesthesia, urinary incontinence, and urinary retention), lymph cyst, lymphedema, ureterovaginal fistula, intestinal obstruction, wound infection, urinary tract infections, and in which bladder dysfunction is the most common. Chronic urinary retention is the accumulation of urine in the bladder that results from incomplete bladder emptying, which is the most common cause of chronic urinary retention. It is measured as the volume of urine left in the bladder after voiding, also known as postvoid residual. The 2 most common causes of chronic urinary retention and incomplete bladder emptying are bladder muscle dysfunction and bladder outlet obstruction. The latter cause is defined as a "generic term for obstruction during voiding." It is less common in women, and the prevalence data range widely, owing to a lack of uniform definition and coexistence of storage and voiding disorders. Any process that compresses the urethra may impair urine flow and result in an obstruction; potential causes include fibroids, constipation, and, uncommonly, cancer.[3–5]

Currently, radical resection of cervical cancer is used as the principal mean for the treatment of early cervical cancer (stage IA to IIA). During the surgical resection of cervical cancer, the pelvic autonomic nerve will be destroyed and part of the nerves that innervate the bladder will be cut off, leading to bladder contraction and sensory dysfunction, as well as urination disorders and urinary retention.[6–8] After the urinary catheter is removed, the patient is unable to urinate successfully, which may lead to urinary tract infection and renal insufficiency in severe cases. In the process of clinical nursing, patients are usually instructed by nurses to urinary retention out intermittent clamping training about 3 days prior to catheter removal to ensure smooth urination after catheter removal. However, practice shows that intermittent pinching training alone is not effective, with unsatisfactory bladder recovery effects for patients. For this reason, new nursing methods are urgently needed to be developed in the clinic to solve the problems of

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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bladder function recovery and urinary retention after radical resection of cervical cancer.[9–11]

Although 3 prospective randomized controlled trials (RCTs) and 1 systematic review with a meta-analysis have been published up to now. they are not enough to clarify the efficacy and safety of NSRS in cervical cancer due to small numbers of enrolled patients and non-English literature that hinder extraction of relevant data. Presently, we pooled data from previously published findings and conducted a meta-analysis to combine results quantitatively. The purpose of this study was to achieve an integrative understanding of the associations between urinary retention in nerve-sparing radical hysterectomy and radical hysterectomy for cervical cancer.

2. Materials and methods

2.1. Selection strategy

Study was selected from databases of PubMed, Embase, Wanfang, and China National Knowledge Internet with the last report up to January 15, 2022. Studies for randomized controlled trials (RCTs) involving independent LNSRH and LRH as the treatment of early stage of cervical cancer based on FIGO staging. Furthermore, print-out literatures were selected by manual retrieval, and the references of reviews and included articles were further retrieved for more included studies.

2.2. Inclusion and exclusion criteria

Studies that met the following criteria were included in the present analysis: prospective or retrospective cohort study; RCT study design; related outcomes and complete data were reported. Studies were excluded if the study included only 1 surgical treatment group without a comparison design. We excluded the studies failing to report the basic study characteristics such as age, body mass index, FIGO stage. Reviews, editorials, guidelines, case reports, letters, and meeting papers were excluded.

2.3. Data extraction quality assessment

Two investigators screened articles independently according to the above inclusion and exclusion criteria. After confirming the inclusion of the analyzed articles, they independently extracted the following data according to a standardized form: the name of the first author, publication year, study area, age and sex of participants, sample size, types of patients, and intervention and complications. After completion of data extraction, the 2investigators checked each other, and the controversies were discussed and resolved.

2.4. Statistical analysis

Hazard ratio (HR) and its 95% confidence interval (CI) were chosen as the evaluation index. Heterogeneity was assessed using Cochran Q test and I^2 test.[12] If $P < .05$ and/or $I^2 > 50\%$ which suggested obvious heterogeneity across studies, the random effects model would be selected to pool data. Otherwise ($P \geq .05$ and $I^2 \leq 50\%$), the fixed effect model was adopted. Additionally, subgroup analysis was conducted based on areas and cancer types (primary and metastatic cancer). an I^2 of > 50% was considered to represent substantial heterogeneity, and thereby we used the random effects model using the Der Simonian and Laird method. On the other hand, the fixed effect model using the Mantel–Haenszel method was employed when I^2 was ≤ 50% because it meant no heterogeneity. Egger test was used to assess whether there was publication bias. Trim and fill method, as well as sensitivity analysis were used to evaluate the stability of results. All the statistical analyses were performed utilizing Stata11.0.

3. Results

3.1. Study selection

As shown in Figure 1, a total of 490 articles in PubMed, 324 articles in Embase, 140 articles in Wanfang, and 39 articles in

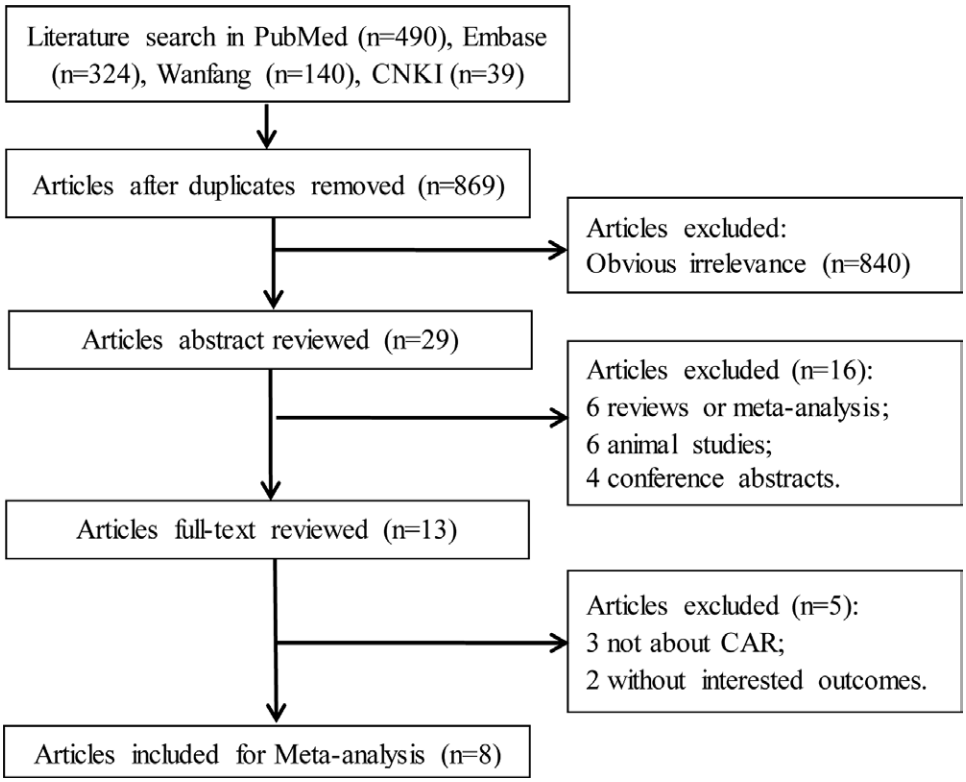

Figure 1. The detailed flow chart for literature search and study selection.

Table 1

Information of references enrolled in this study.

Study	Area	Type of cancer, Stage	n, M/F	Age, yr	Intervention	Cut off value of CAR	Follow-up period, yr	OS (high vs low)	DFS (high vs low)	Adjusted factors
Asher 2011	China	Primary cancer, I-IV	163, 106/57	55 (15–81)	Chemotherapy or Surgery	0.132	8	1.30 (1.11, 1.52)	NR	None
Cho 2009	Japan	Metastatic cancer, NR	106, 76/30	64.5 (39–87)	Hepatic resection	0.04	10	2.56 (1.42, 4.61)	1.73 (1.09, 2.76)	Number of regional lymph node metastases, status of neoadjuvant chemotherapy
Feng 2016	China	Primary cancer, I–III	115, 82/33	64 (33–83)	Chemoradioth-era-py followed by Surgery	0.049	5.5	5.09 (2.31, 11.58)	4.98 (2.34, 11.14)	Pretreatment TNM stage, Pathological TNM tage, Vascular invasion, Pretreatment CEA
Kwon BS 2018	South Korea	Primary cancer, I–IV	627, 400/227	67 ± 12	Surgery	0.038	2.5	2.61 (1.62, 4.21)	NR	Gender, Maximum tumor diameter, Tumor type, Pathological differentiation, WBC count, Platelet count, CEA, CA19-9, NLR, GPS, Stage
Miao 2016	China	Metastatic cancer, IV	148, 97/51	NR	Chemotherapy	0.6712	5	1.59 (1.28, 1.99)	NR	Gender, Age, Location of primary tumor, Metastasis number, Hemoglobin, Globulin, GPS, mGPS, NLR, PLR, MLR
Thvaramara 2011	Japan	Metastatic cancer, NR	99, 57/42	63 (27–86)	Chemotherapy	0.183	1.7	1.87 (1.06, 3.30)	NR	Detection of unresectable tumor, the number of organs affected by metastasis, CEA, Molecular targeted therapy, Pretreatment NLR
Wang 2015	China	Primary cancer, I–III	705, 411/294	68 (26–90)	Surgery	0.0271	5	NR	1.50 (1.05, 2.14)	Stage, Tumor diameter, Lymphatic involvement, Venous involvement, Lymph node metastasis
Wang, 2016	China	Primary cancer, III	136, 79/57	63.5	Chemotherapy with Colorectal resection	0.1	9	1.15 (0.91, 1.44)	4.43 (1.94–10.15)	Tumor size, Vessel invasion, NLR
Williams 2014										
Zhang 2015	China									

CAR = C-reactive protein/albumin ratio, DFS = disease-free survival, F = female, GPS = Glasgow prognostic score, M = male, MLR = monocyte-to-lymphocyte ratio, NR = not reported, NLR = neutrophil-to-lymphocyte ratio, OS = overall survival, PLR = platelet-to-lymphocyte ratio.

China National Knowledge Internet were selected. Subsequent to excluding any duplicates, 869 articles remained. Then 840 irrelevant articles were removed by reviewing the titles. After reading the abstract, 16 articles were excluded. By fully reviewing the articles, 5 articles were removed. Finally, 8 articles were included in the meta-analysis.[13–20]

3.2. Characteristics of the included studies

The characteristics of the enrolled studies are presented in Table 1. All studies were retrospective cohort studies. The areal distributions were China (2 articles) and Japan (6 articles). Quality assessment demonstrated that the quality of the included studies was relatively high (total quality scores ≥ 6) (Table 2).

3.3. Meta-analysis

Meta-analysis of urinary retention showed that there was a significant correlation between NSRH and RH treatments of cervical cancer patients (HR [95% CI] = 1.78 [1.37, 2.31], P < .001). Egger test identified a significant publication bias (P = .014). After supplementing 3 studies with trim and fill method, the pooled fixed effect model was HR (95% CI) = 1.35 (1.22, 1.49), P < .001, and the random effects model was HR (95% CI) = 1.39 (1.06, 1.83), P = .019. Sensitivity analysis revealed that after successively removing 1 study, the pooled results ranged from 1.60 (1.27, 2.00) to 1.99 (1.41, 2.82), with significant differences, which suggested that results were statistically reliable (Fig. 2).

As shown in Figure 3, meta-analysis of urinary retention revealed a significant correlation between NSRH and RH treatments of cervical cancer patients (HR [95% CI] = 2.49 [1.43, 4.33], P = .001). Significant publication bias was revealed via Egger test (P = .017). After 1 study was supplemented with trim and fill method, the pooled results were fixed effect model being HR (95% CI) = 1.80 (1.42, 2.29), P < .001 and random effects model being HR (95% CI) = 2.06 (1.20, 3.51), P = .008. Sensitivity analysis by omitting 1 study at each time showed that the pooled result ranged from 1.99 (1.22, 3.27) to 3.17 (1.50, 6.70), and omission of any study made a significant difference (P < .05), indicating statistical reliability and good stability of our results.

Table 2

Quality assessment of the included studies with Newcastle-Ottawa quality assessment scale.

Study	Representativeness of the exposed cohort	Selection of the unexposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Control for important factor or additional factor	Outcome assessment	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total quality scores
Chen YY (2017)	☆	☆	☆	--	--	☆	☆	☆	6
Haruki, K (2017)	☆	☆	☆	--	☆☆	☆	☆	☆	8
Ide, S (2017)	☆	☆	☆	--	☆☆	☆	☆	☆	8
Ishizuka, M (2016)	☆	☆	☆	--	☆☆	☆	--	☆	7
Ni, XF (2016)	☆	☆	☆	--	☆☆	☆	☆	☆	8
Shibutani, M (2016a)	☆	☆	☆	--	☆☆	☆	--	☆	7
Shibutani, M (2016b)	☆	☆	☆	--	☆☆	☆	☆	☆	8
Tominaga, T (2016)	☆	☆	☆	--	☆	☆	☆	☆	7

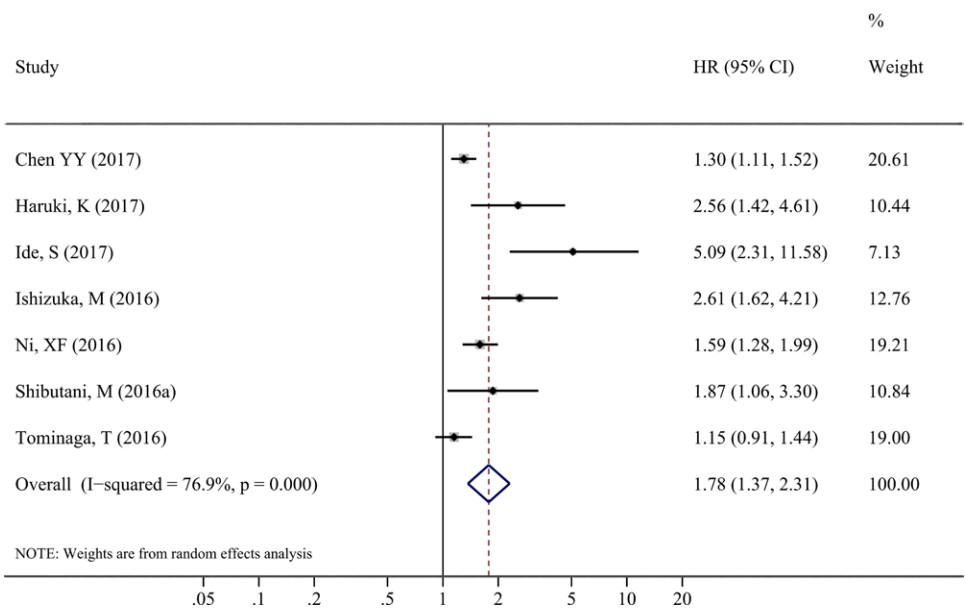

Figure 2. Meta-analysis of correlation of urinary retention between NSRH and RH treatments of cervical cancer patients.

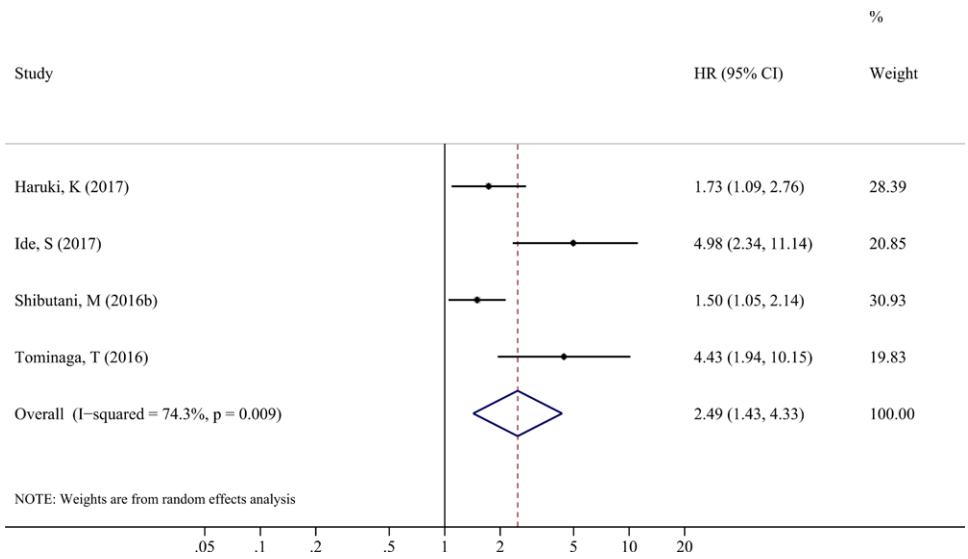

Figure 3. Meta-analysis of correlation between NSRH and RH treatments of cervical cancer patients.

3.4. Subgroup analysis

The results of subgroup analysis are shown in Table 3. In the subgroup analysis of urinary retention, the pooled results of 2 areas and 2 types of cancer had statistical significances. There were significant heterogeneities in subgroups of China, Japan, and primary cancer. In the subgroup analysis of urinary retention, all studies were Japanese, and the pooled results of type of cancer had significant difference. Primary cancer subgroup had significant heterogeneity.

4. Discussion

In our study, we combined 8 retrospective cohort studies. Meta-analysis of urinary retention showed a significant correlation between NSRH (HR [95% CI] = 1.78 [1.37, 2.31], $P < .001$) and RH treatments (HR [95% CI] = 2.49 [1.43, 4.33], $P = .001$) of cervical cancer patients.

To the best of our knowledge, this study is the first to systematically assess the association between urinary retention and prognosis in patients with cervical cancer. The included studies had moderate methodological quality, making our analysis result reliable.[21–23] Moreover, the stability of the results was good despite the significant publication bias. However, there were several limitations in this study that should be acknowledged. One the 1 hand, the number of included studies was small and significant between-study heterogeneity was detected. On the other hand, we performed subgroup analysis in order to reduce the heterogeneity. However, the heterogeneities between subgroups were significant as well, therefore, we cannot find the source of heterogeneity based on quantitative analysis.

NSRH was also believed to have better anorectal function in cervical cancer survivors. Although anorectal function outcomes were reported by several studies, we only found 2 relevant studies with comparable data on anorectal dysfunction.[24,25] Due to various parameters indicating anorectal dysfunction such as constipation, defecation straining, stool incontinence and flatulence incontinence, and we chose constipation as the comparable parameter of anorectal dysfunction in this review. However, meta-analysis of anorectal dysfunction data of the 2 studies showed no significant difference between NSRH and RH, which might be due to the relatively small number of studies and participants. Since there was only 1 clinical trial with comparable data of the mean time of first flatus and first defecation, which indicated anorectal function recovery, we couldn't meta-analysis these data.[26]

In conclusion, there is a significant correlation urinary retention revealed a significant correlation between NSRH and RH treatments of cervical cancer patients Further rigorous and high-quality sample study should be designed to verify the correlation.

Author contributions

Conceptualization: Jing Zhou.
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Formal analysis: Jing Zhou, Rong Zhang, Xiajuan Jiang.
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Investigation: Xiaohui Tang, Suwei Liu.
Methodology: Suwei Liu.
Visualization: Xiajuan Jiang.
Writing – original draft: Jing Zhou, Xiajuan Jiang.
Writing – review & editing: Jing Zhou, Xiajuan Jiang.

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