Primary Treatment for Clinically Early Cervical Cancer with Lymph Node Metastasis: Radical Surgery or Radiation?*

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[Abstract] Objective: To compare survival outcomes between primary radical surgery and primary radiation in early cervical cancer. **Methods:** Patient information was extracted from the Surveillance, Epidemiology, and Results database. Patients diagnosed with early cervical cancer of stage T1a, T1b, and T2a (American Joint Committee on Cancer, 7th edition) from 1998 to 2015 were included in this study after propensity score matching. Overall survival (OS) was analyzed using the Kaplan-Meier method. **Results:** Among the 4964 patients included in the study, 1080 patients were identified as having positive lymph nodes (N1), and 3884 patients were identified as having negative lymph nodes (N0). Patients with primary surgery had significantly longer 5-year OS than those with primary radiotherapy in both the N1 group (P<0.001) and N0 group (P<0.001). In the subgroup analysis, similar results were found in patients with positive lymph nodes of stage T1a (100.0% *vs*. 61.1%), T1b (84.1% *vs*. 64.3%), and T2a (74.4% *vs*. 63.8%). In patients with T1b1 and T2a1, primary surgery resulted in longer OS than primary radiation, but not in patients with T1b2 and T2a2. In multivariate analysis, the primary treatment was identified as an independent prognostic factor in both N1 and N0 patients (HR_{N1}=2.522, 95% CI=1.919–3.054, P_{N1}<0.001; HR_{N0}=1.895, 95% CI=1.689–2.126, P_{N0}<0.001). **Conclusion:** In early cervical cancer stage T1a, T1b1, and T2a1, primary surgery may result in longer OS than primary radiation for patients with and without lymph node metastasis.

Key words: early cervical cancer; overall survival; primary treatment; lymph node status; radical surgery; radiation

Cervical cancer is the fourth most common cancer in women worldwide and remains a global challenge. According to global cancer statistics, there were estimated 569 847 new cases and 311 365 deaths in 2018[1]. Among all cases of cervical cancer, the 5-year disease-free survival rates of patients diagnosed with early-stage cervical cancer exceeded 90% in some studies[2].

For patients with early cervical cancer, the standard treatment is either radical hysterectomy with pelvic lymphadenectomy or radiation[3]. Although lymph node metastases (LNM) in clinically early-stage disease are relatively rare[4], they have been identified as one of the most critical prognostic factors[5]. Once LNM occurs, the 5-year survival rate of patients with positive lymph nodes decreases by 28% compared to patients with negative nodes[6]. The new International Federation of Gynecology and Obstetrics (FIGO) staging criteria released in 2018 integrated pelvic and para-aortic lymph node metastasis in the classification of cervical cancer[7], which illustrates that lymph node metastasis status is related to cervical cancer prognosis.

Traditionally, positive nodes are detected by systematic pelvic lymphadenectomy as an integral part of radical surgery, and for patients with LNM, postoperative radiotherapy is mandatory. In the last decade, sentinel lymph node (SLN) mapping has been increasingly used for LNM staging of cervical cancer, which allows the diagnosis of LNM with acceptable

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accuracy before radical hysterectomy. However, there is no consensus on whether radical surgery should be abandoned or completed if positive nodes are found during surgery in patients with clinically early-stage cervical cancer. In an international survey investigating the practice patterns among centers and physicians regarding the treatment of cervical cancer patients with positive SLN biopsy, 39% of respondents stopped surgery and subjected patients to chemoradiation, 45% completed pelvic and paraaortic lymphadenectomy, and 26% completed radical hysterectomy and systematic lymphadenectomy[8]. The dilemma of whether to omit radical surgery in patients with LNM originates from concerns about how to balance the potential benefits and harms of the treatment. On the one hand, radical surgery followed by radiation may be associated with a higher risk of postoperative complications than radiation alone. On the other hand, radical surgery may yield additional survival benefits by reducing tumor burden. Thus, it is important to determine whether radical surgery or radiotherapy is more beneficial for the survival of cervical cancer patients with LNM.

In the present study, we analyzed the overall survival (OS) rate in patients with clinically early-stage cervical cancer stratified by node status and primary treatment using real-world data from The Surveillance, Epidemiology, and Results (SEER) program of the National Cancer Institution. Our data shed light on how to choose the proper treatment strategy for patients with intra-operative detected LNM.

1 MATERIALS AND METHODS

1.1 Data Source

Patient information used in this retrospective study was extracted from the SEER database with permission. The SEER program of the National Cancer Institution is an authoritative source of long-term cancer incidence and survival in the United States (US) and covers approximately 28% of the US population. SEER provides information on cancer statistics including incidence, population data of age, sex, race, year of diagnosis, geographic areas (including SEER registry and country), primary tumor site, stage at diagnosis, first course of treatment, and follow-up for survival. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

1.2 Inclusion Criteria for Patients with Clinically Early-stage Cervical Cancer

This was a retrospective, population-based cohort study. The following inclusion criteria were used: 1) having been diagnosed with primary cervical cancer of stage T1a, T1b, and T2a from 1988 to 2015; 2) histology showing squamous cancer, adenocarcinoma, and adenosquamous cancer depending on ICD-O-3 classification; and 3) having undergone radical surgery and/or radiotherapy as primary treatment.

Patients were excluded if they had metastatic disease, unconfirmed or unknown tumor information, unclear sequence of surgery and radiotherapy, neoadjuvant chemotherapy, or no exact information of survival months or vital status.

1.3 Clinical Features

The following information was collected from the database: age, race, marital status, registry area, year at diagnosis, TNM stage, histology, histologic grade, surgical method, radiotherapy and radiation sequence, chemotherapy, survival months, and vital status. American Joint Committee on Cancer (AJCC) cancer staging 6th edition (cases from 2003 to 2009) and AJCC cancer staging 3rd edition (cases from 1988 to 2002) data were restaged according to the 7th edition of AJCC cancer staging based on the SEER recording information.

The clinical features were grouped as follows: age: <40, 40–49, 50–59, 60–69, or ≥70 years old; race: white, black, Asian, or other races; marital status: married, single, or others; registry area: central, east, or west; year at diagnosis: before 2002, 2003–2009, or 2010/later; histology: squamous, adenocarcinoma, or adenosquamous; histologic grade: Ⅰ, Ⅱ, Ⅲ/Ⅳ, or unknown; treatment: primary radical surgery or primary radiation; lymph node metastasis status: N0 or N1.

1.4 Statistical Analysis

All statistical analyses were performed using SPSS (version 26.0). Propensity score matching (PSM) was applied to control for confounding factors. In our study, treatment (surgery or radiotherapy) was used as the dependent variable, and confounding factors (age, race, marital status, registry area, year at diagnosis, T stage, histology, histologic grade, and chemotherapy) were used as covariates in 1:1 PSM. The PSM procedure was performed using the SPSS PSM plug-in "ps matching". The statistical significance of baseline clinical-pathological characteristics was assessed with the χ^2 test or Fisher's exact test, as appropriate. Survival analysis was performed with the Kaplan-Meier method, and the log-rank test was used to assess the differences. Variables in univariate and multivariate analyses were screened using Cox regression analysis. $P<0.05$ was considered statistically significant.

2 RESULTS

2.1 Overall Cohort Characteristics

The composition of the study population and consecutive processes of sample matching are depicted in fig. 1. Of 94 177 SEER cervical cancer cases diagnosed between 1998 and 2015, 20 830 had histologically confirmed cervical cancer with adequate survival, TNM, and treatment data, of whom 18 207 had

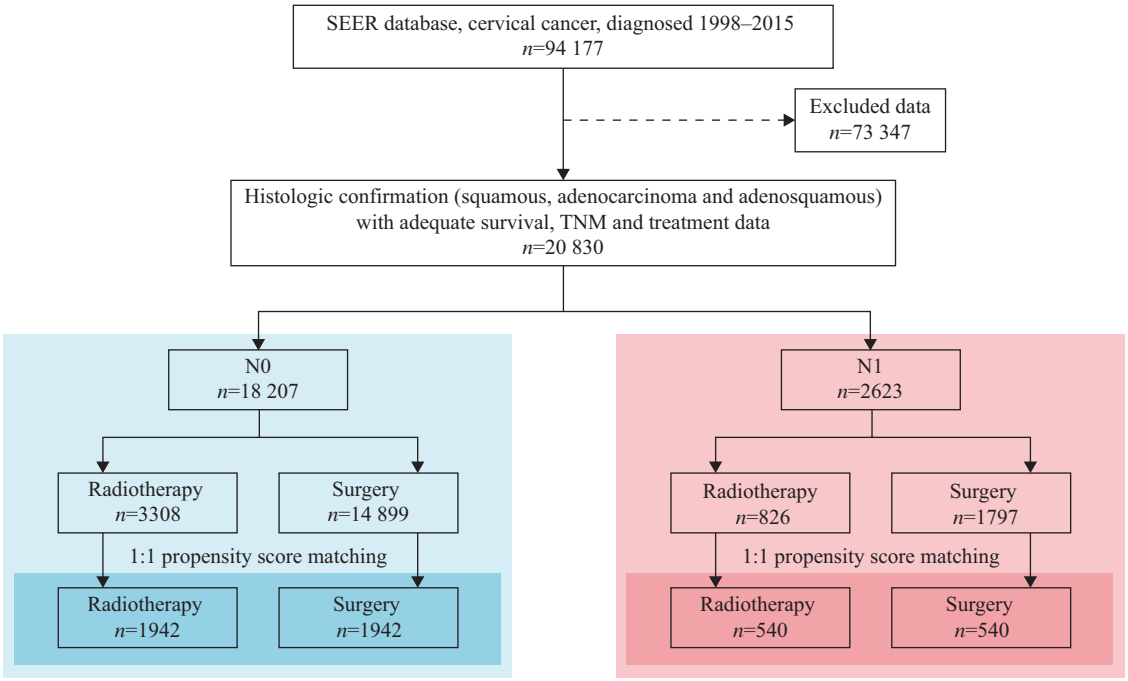

Fig. 1 Flow diagram depicting the composition of the study population and consecutive processes of sample matching
N0, patients with negative lymph nodes; N1, patients with positive lymph nodes

N0 (negative lymph nodes) disease and 2636 had N1 (positive lymph nodes) disease. To overcome imbalance in the sample size and baseline characteristics between the primary radiation and primary surgery groups, we conducted 1:1 PSM, considering the proportion of primary radiation and primary surgery groups.

2.2 Baseline Characteristics of Patients

A total of 20 830 patients registered in the SEER database were included before PSM (table S1). PSM was applied to control for confounding factors (table 1). One thousand and eighty patients were identified with positive lymph nodes based on N stage in the SEER database (N1 group), including 540 patients with primary surgery (N1-S group) and 540 patients with primary radiotherapy (N1-R group). In addition, 3884 patients were identified with negative lymph nodes (N0 group), including 1942 patients with primary radical surgery (N0-S group) and 1942 with primary radiotherapy (N0-R group).

2.3 Effect of Primary Treatment on OS

The median follow-up time was 65.51 months. In the N1 group, patients who underwent primary surgery had significantly longer 5-year OS than patients who received primary radiation (82.2% *vs*. 64.1%, $P<0.001$, fig. 2A). Multivariate analysis showed that radiation was an independent risk factor for OS [hazard ratio (HR)=2.522, 95% confidence interval (CI)=1.996–3.187, $P<0.001$, table 2]. Additional variables associated with OS were age, race, histopathology, and chemotherapy (table 2). Similarly, N0-S patients had better 5-year OS than N0-R patients (83.1% *vs*. 70.0%, $P<0.001$, fig. 2A), and radiation was an independent risk factor (HR=1.895, 95% CI=1.689–2.126, $P<0.001$, table 3).

2.4 Subgroup Analysis by Tumor Stage

Subgroup analysis was performed to determine whether primary radical surgery results in longer survival in all early stages of cervical cancer. The curves in fig. 2 show a longer OS in patients with primary radical surgery than in patients treated with radiation in both the N0 and N1 groups (fig. 2A–2D). In all three groups of stage T1a, T1b, and T2a tumors, N0-S patients achieved a longer 5-year OS than N0-R patients ($P<0.001$, fig. 2B–D). For patients with positive lymph nodes, a significant difference was observed in the 5-year OS of T1a ($P<0.001$), T1b ($P<0.001$), and T2a ($P=0.007$) groups. The results before PSM showed that there was a significant difference in survival rate between the two treatment modalities ($P=0.001$, fig. S1A–1D).

It is believed by some scholars that concurrent chemoradiation (CCRT) should be recommended for patients with bulky tumors, especially those with positive lymph nodes[3, 9]. This shows that tumor size is also one of the factors related to the prognosis of cervical cancer that cannot be ignored. To test this, a more precise T stage was divided into T1b1, T1b2 and T2a1, T2a2 according to the database, where the tumor size of T1b1, T2a1 was <4 cm and that of T1b2, T2a2 was >4 cm. The results showed that in patients with T1b1 and T2a1 (tumor <4 cm) and positive lymph nodes, primary surgery resulted in longer OS than primary radiation (fig. 3A, 3C). However, there was no significant difference in survival between the surgery

Table 1 Baseline characteristics of included patients with early-stage cervical cancer

	N1 (*n*=1080)			N0 (*n*=3884)		
	Radiotherapy (*n*=540)	Surgery (*n*=540)	*P*-value	Radiotherapy (*n*=1942)	Surgery (*n*=1942)	*P*-value
T stage			0.977			0.152
T1a	18 (3.3%)	18 (3.3%)		124 (6.4%)	116 (6.0%)	
T1b	392 (72.6%)	389 (72.0%)		1465 (75.4%)	1515 (78.0%)	
T2a	130 (24.1%)	133 (24.6%)		353 (18.2%)	311 (16.0%)	
Age (years)			0.997			0.386
<40	188 (34.8%)	184 (34.1%)		437 (22.5%)	405 (20.9%)	
40–49	150 (27.8%)	150 (27.8%)		523 (26.9%)	510 (26.3%)	
50–59	111 (20.6%)	113 (20.9%)		371 (19.1%)	378 (19.5%)	
60–69	61 (11.3%)	64 (11.9%)		285 (14.7%)	280 (14.4%)	
≥70	30 (5.6%)	29 (5.4%)		326 (16.8%)	369 (19.0%)	
Race/ethnicity			0.364			0.878
White	428 (79.3%)	407 (75.4%)		1461 (75.2%)	1483 (76.4%)	
Asian	31 (5.7%)	43 (8.0%)		152 (7.8%)	145 (7.5%)	
Black	68 (12.6%)	73 (13.5%)		284 (14.6%)	271 (14.0%)	
Others	13 (2.4%)	17 (3.1%)		45 (2.3%)	43 (2.2%)	
Marital status			0.738			0.885
Single	181 (33.5%)	169 (31.3%)		481 (24.8%)	489 (25.2%)	
Married	233 (43.1%)	241 (44.6%)		826 (42.5%)	832 (42.8%)	
Others	126 (23.3%)	130 (24.1%)		635 (32.7%)	621 (32.0%)	
Registry area			0.762			0.426
West	266 (49.3%)	277 (51.3%)		936 (48.2%)	943 (48.6%)	
Central	111 (20.6%)	110 (20.4%)		415 (21.4%)	384 (19.8%)	
East	163 (30.2%)	153 (28.3%)		591 (30.4%)	615 (31.7%)	
Year at diagnosis			0.969			0.928
Before 2002	37 (6.9%)	36 (6.7%)		434 (22.3%)	444 (22.9%)	
2003–2009	224 (41.5%)	221 (40.9%)		826 (42.5%)	822 (42.3%)	
2010 or later	279 (51.7%)	283 (52.4%)		682 (35.1%)	676 (34.8%)	
Histology			0.755			0.269
Adenocarcinoma	80 (14.8%)	87 (16.1%)		377 (19.4%)	412 (21.2%)	
Adenosquamous	33 (6.1%)	29 (5.4%)		96 (4.9%)	105 (5.4%)	
Squamous	427 (79.1%)	424 (78.5%)		1469 (75.6%)	1425 (73.4%)	
Histologic grade			0.903			0.117
Ⅰ	23 (4.3%)	25 (4.6%)		143 (7.4%)	160 (8.2%)	
Ⅱ	199 (36.9%)	191 (35.4%)		679 (35.0%)	680 (35.0%)	
Ⅲ, Ⅳ	255 (47.2%)	265 (49.1%)		735 (37.8%)	771 (39.7%)	
Unknown	63 (11.7%)	59 (10.9%)		385 (19.8%)	331 (17.0%)	
Chemotherapy			0.616			0.463
No/unknown	58 (10.7%)	53 (9.8%)		718 (37.0%)	696 (35.8%)	
Yes	482 (89.3%)	487 (90.2%)		1224 (63.0%)	1246 (64.2%)	

N0, patients with negative lymph nodes; N1, patients with positive lymph nodes

and radiation groups for patients of T1b2 and T2a2 (tumor >4 cm), regardless of the status of lymph nodes (fig. 3B, 3D).

3 DISCUSSION

Due to the controversy regarding primary treatment for early cervical cancer with positive lymph node status, we conducted this retrospective study to compare the efficacy of primary radical surgery and radiation on survival in patients with early cervical cancer with or without lymph node metastasis. Propensity score analysis was conducted in our study to adjust for confounders and facilitate comparability between subgroups. Our data showed that the primary treatment modality was an independent prognostic factor for early cervical cancer, and primary surgery resulted in longer survival time than radiation in patients (T1a, T1b1, and T2a1) both with and without lymph node metastasis. This study provides important evidence for the treatment of early cervical cancers.

The main controversy around primary treatment strategy is centered on the treatment of nonbulky cervical cancers with positive lymph nodes. Several studies have compared the efficacy of radical surgery and radiation in patients with early cervical cancer. In

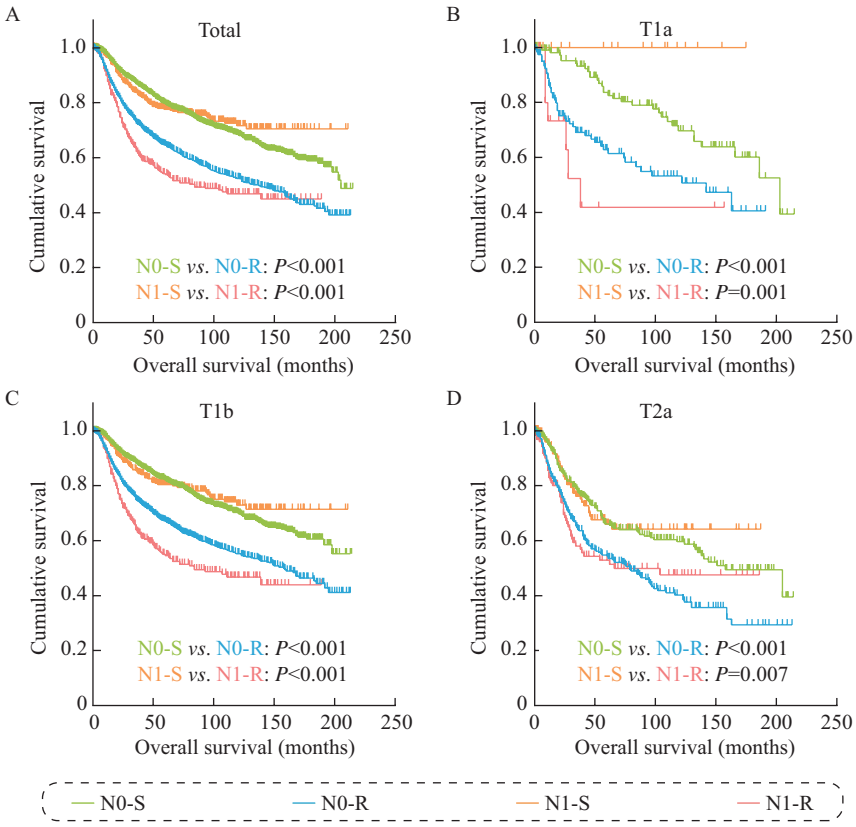

Fig. 2 Kaplan-Meier overall survival (OS) curves of all patients
OS of total patlents (A) and patients with stage T1a (B), T1b (C) and T2a (D) disease according to the primary treatment and status of lymph nodes

a retrospective study with stage IB1 cervical cancers, Doll *et al* observed significantly longer progression-free survival and OS in patients who underwent radical surgery than in those who underwent radiation (P<0.001)[10]. In another retrospective study based on data from the SEER database, Bansal also discovered that radical surgery was associated with a 62% reduction in mortality (HR=0.38, 95% CI=0.30–0.48) in patients with tumors <4 cm[11]. The conclusions of these studies are consistent with ours, but there are some other studies that failed to show additional benefit of primary surgery when compared to primary radiotherapy. Hopkins *et al* reported no significant difference in survival when comparing radical surgery to radiation therapy (92% *vs*. 86%, P=0.098)[12]. However, none of these studies gave prominence to the status of lymph nodes, which is one of the most important risk factors for prognosis[13]. In 2018, the FIGO revised the 2014 FIGO staging system of cervical cancer. The updated staging system defined patients with regional lymph node metastasis as stage ⅢC[14]. However, Grigsby *et al* restaged patients with stage ⅢC1 disease (positive pelvic lymph nodes staged by their FIGO 2018) according to the AJCC 7th edition T stage[15]. The 5-year progression-free survival rates were 72% in T1, 63% in T2, and 41% in T3 (P<0.0001), indicating that the survival rate of patients with positive lymph nodes differed with tumor size[15]. In this study, for nonbulky cervical cancer (tumor ≤4 cm, T1b1 and T2a1) with positive lymph nodes, we also observed significantly longer OS in patients with primary radical surgery than in those with primary radiation. For patients with bulky tumors (tumor >4 cm, T1b2 and T2a2), there was no significant difference in survival between the surgery and radiation groups. Therefore, whether the lymph node status should be the only standard when staging and choosing the treatment remains controversial.

The ESGO/ESTRP/ESP guideline and some clinicians recommend lymph node assessment, such as SLN mapping/biopsy or imaging, to determine treatment strategy[16]. SLN mapping combined with ultra-staging has been considered an alternative to systematic lymphadenectomy with an acceptable accuracy of LNM detection and has been increasingly used in the management of early-stage cervical cancer[17]. However, due to the discrepancies in the current studies and lack of consensus, the treatment strategy for patients with positive sentinel lymph node biopsy (SLNB) was determined by experience or personal preference. Therefore, the optimal treatment of SLNB-positive cases of cervical cancer is still controversial. In this study, we focused on the treatment for patients at different stages with positive lymph nodes. We found that, in early cervical cancer

Table 2 Cox analysis of overall survival in patients with positive lymph nodes

Variables	*n*	Univariate		Multivariate	
		HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
T stage					
T1a	36	1			
T1b	781	1.367 (0.644–2.901)	0.415		
T2a	263	1.717 (0.794–3.712)	0.169		
Age (years)					
<40	372	1		1	
40–49	300	0.968 (0.723–1.295)	0.825	0.931 (0.693–1.252)	0.638
50–59	224	1.225 (0.899–1.668)	0.198	1.231 (0.902–1.680)	0.190
60–69	125	1.369 (0.949–1.975)	0.093	1.430 (0.985–2.075)	0.060
≥70	59	2.169 (1.427–3.297)	0.000	2.119 (1.381–3.251)	0.001
Race/ethnicity					
White	835	1		1	
Asian	74	0.694 (0.418–1.152)	0.158	0.719 (0.432–1.197)	0.205
Black	141	1.394 (1.046–1.858)	0.024	1.496 (1.114–2.010)	0.007
Others	30	0.995 (0.492–2.014)	0.989	1.260 (0.618–2.567)	0.525
Marital status					
Single	350	1			
Married	474	0.830 (0.640–1.077)	0.161		
Others	256	1.168 (0.878–1.555)	0.287		
Registry area					
West	543	1			
Central	221	1.054 (0.790–1.407)	0.720		
East	316	1.149 (0.892–1.479)	0.283		
Year at diagnosis					
Before 2002	73	1			
2003–2009	445	0.941 (0.640–1.385)	0.759		
2010 or later	562	1.013 (0.676–1.517)	0.952		
Histology					
Adenocarcinoma	167	1		1	
Adenosquamous	62	0.718 (0.430–1.200)	0.206	0.658 (0.392–1.104)	0.113
Squamous	851	0.640 (0.485–0.846)	0.002	0.641 (0.482–0.853)	0.002
Histologic grade					
Ⅰ	48	1			
Ⅱ	390	0.885 (0.505–1.553)	0.671		
Ⅲ, Ⅳ	520	1.306 (0.758–2.253)	0.336		
Unknown	122	1.122 (0.609–2.067)	0.711		
Chemotherapy					
No/unknown	111	1		1	
Yes	969	0.666 (0.483–0.918)	0.013	0.697 (0.501–0.969)	0.032
Treatment					
N1+S	540	1		1	
N1+R	540	2.421 (1.919–3.054)	<0.001	2.522 (1.996–3.187)	<0.001

N1+R, patients with positive lymph nodes who received primary radiation; N1+S, patients with positive lymph nodes who received primary radical surgery

of T1a, T1b1, and T2a1 (ⅠB1 and ⅡA1, grouped by FIGO 2009 tumor stage) identified with positive lymph nodes, primary surgery resulted in better outcomes than radiation for nonbulky tumors, whereas survival was comparable in surgery and radiation groups for patients with bulky tumors of both stages T1b2 and T2a2 (ⅠB2 and ⅡA2, grouped by FIGO 2009 tumor stage). This indicates that the involvement of lymph nodes status may not be the only standard for treatment choice, and primary tumor size should also be comprehensively considered. Primary radical surgery may remove the lesions and afford accurate pathological features that permit better targeting of adjuvant therapy, allowing individualization of therapy[18], as well as the therapeutic value of lymphadenectomy and removal of primary lesions[19, 20], whereas pelvic lymph node involvement and residual disease may persist in some patients after radiation.

There are some limitations to our analysis. We lacked individual-level information on variables such

Table 3 Cox analysis of overall survival in patients with negative lymph nodes

Variables	*n*	Univariate		Multivariate	
		HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
T stage					
T1a	240	1		1	
T1b	2980	0.927 (0.737–1.165)	0.514	1.076 (0.851–1.36)	0.541
T2a	664	1.478 (1.152–1.896)	0.002	1.538 (1.192–1.985)	<0.001
Age (years)					
<40	842	1		1	
40–49	1033	0.916 (0.758–1.107)	0.366	0.963 (0.796–1.166)	0.701
50–59	749	1.103 (0.905–1.344)	0.331	1.136 (0.928–1.389)	0.217
60–69	565	1.496 (1.225–1.826)	<0.001	1.494 (1.214–1.840)	<0.001
≥70	695	3.099 (2.617–3.668)	<0.001	3.11 (2.551–3.790)	<0.001
Race/ethnicity					
White	2944	1		1	
Asian	297	0.835 (0.662–1.054)	0.130	0.692 (0.545–0.880)	0.003
Black	555	1.239 (1.067–1.439)	0.005	1.133 (0.967–1.327)	0.122
Others	88	0.973 (0.659–1.437)	0.890	1.107 (0.748–1.639)	0.611
Marital status					
Single	970	1		1	
Married	1658	0.75 (0.647–0.871)	<0.001	0.709 (0.608–0.828)	<0.001
Others	1256	1.318 (1.142–1.520)	<0.001	0.894 (0.764–1.045)	0.159
Registry area					
West	1879	1		1	
Central	799	1.188 (1.028–1.372)	0.019	1.236 (1.065–1.434)	0.005
East	1206	1.151 (1.011–1.309)	0.033	1.126 (0.983–1.291)	0.086
Year at diagnosis					
Before 2002	878	1		1	
2003–2009	1648	0.837 (0.736–0.952)	0.007	0.89 (0.781–1.015)	0.082
2010 or later	1358	0.791 (0.664–0.941)	0.008	0.857 (0.717–1.024)	0.089
Histology					
Adenocarcinoma	789	1			
Adenosquamous	201	0.939 (0.702–1.257)	0.673		
Squamous	2894	1.145 (0.989–1.327)	0.071		
Histologic grade					
Ⅰ	303	1		1	
Ⅱ	1359	1.164 (0.915–1.479)	0.216	1.134 (0.890–1.443)	0.308
Ⅲ, Ⅳ	1506	1.362 (1.076–1.723)	0.010	1.366 (1.078–1.731)	0.010
Unknown	716	1.118 (0.867–1.443)	0.390	1.026 (0.793–1.326)	0.846
Chemotherapy					
No/unknown	1414	1		1	
Yes	2470	0.569 (0.508–0.636)	<0.001	0.904 (0.788–1.037)	0.148
Treatment					
N0+S	1942	1		1	
N0+R	1942	1.799 (1.605–2.017)	<0.001	1.895 (1.689–2.126)	<0.001

N0+R, patients with negative lymph nodes who received primary radiation; N0+S, patients with negative lymph nodes who received primary radical surgery

as smoking, alcohol, medication use, and obesity, which may contribute to the risk of death from both surgery and radiotherapy causes. Differences in the approach to coding treatment and TNM status between populations may have resulted in some misclassification, although we expect any impact on study results to be minimal. Additionally, we only investigated the relationship between primary treatment (surgery or radiation) and survival, while primary treatment, such as CCRT and neoadjuvant chemotherapy, was not further grouped. Therefore, further studies are still needed.

In conclusion, the present study suggests that primary surgery may provide longer survival than radiation in patients with early-stage cervical cancer (with stage T1a, T1b1, and T2a1) with either positive or negative lymph nodes.

Conflict of Interest Statement

The authors declare that there is no conflict of interest with any financial organization or corporation or individual that can inappropriately influence this work.

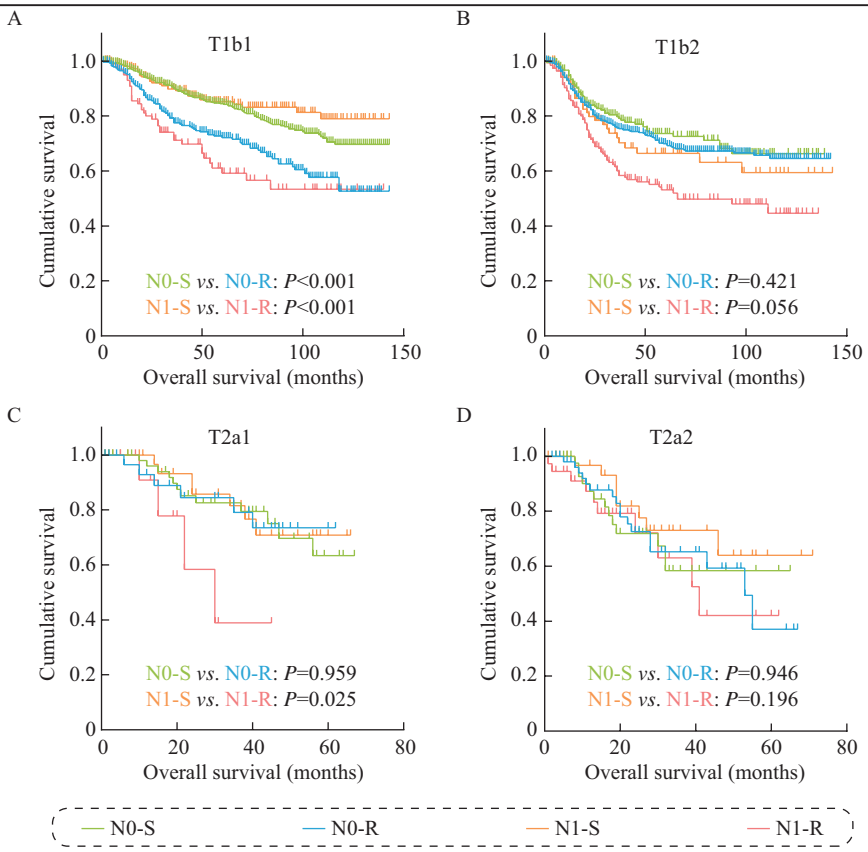

Fig. 3 Kaplan-Meier overall survival (OS) curves of patients in subgroups of stage T1b and T2a according to primary treatment and status of lymph nodes
A: OS curves of patients with T1b1; B: OS curves of patients with T1b2; C: OS curves of patients with T2a1; D: OS curves of patients with T2a2

Author Ze-hua WANG is a member of the Editorial Board for [Current Medical Science]. The paper was handled by the other editors and has undergone rigorous peer review process. Author Ze-hua WANG was not involved in the journal's review of, or decisions related to, this manuscript.

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