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ORIGINAL RESEARCH

Long-Term Outcomes of Local Tumor Destruction/Excision Versus Total Hysterectomy for Stage IA Cervical cancer: A Retrospective Study Based on the SEER Database

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Background: A growing number of patients with early-stage cervical cancer opt for local tumor resection to preserve the uterus. Nevertheless, there is still a dearth of long-term comparisons between local tumor destruction/excision (LTD/LTE) and total hysterectomy(TH), and the optimal target population for local tumor excision remains uncertain.
Methods: A multicenter retrospective study utilizing the Surveillance, Epidemiology, and End Results (SEER) database to compare the long-term outcomes between LTD/LTE and TH in stage IA cervical cancer patients was conducted. A 1:1 propensity score matching (PSM) method was employed to obtain matched cohorts with similar baseline characteristics in the LTD/LTE and TH groups. Kaplan-Meier analysis was used to compare overall survival (OS) and cancer-specific survival (CSS) between the two groups. The Cox proportional hazard models were employed to identify factors associated with OS and CSS.
Results: This study comprised a total of 6382 cervical cancer patients, with 1759 undergoing LTD/LTE and 4623 undergoing TH. After PSM, a significant difference was observed in OS (P=0.030) between the two groups, while no significant difference was found in CSS (P=0.110). Subgroup analysis of patients with stage IA1 (OS: P=0.018; CSS: P=0.230) and IA2 (OS: P=0.071; CSS: P=0.240) revealed no significant differences in OS and CSS between the two groups. Older age (≥50 years) [HR=2.20; 95% CI: 2.20–3.30)] and histological types other than squamous cell carcinoma and usual-type adenocarcinoma [HR=4.40; 95% CI:1.80–11.10] favored TH for better OS, whereas well-differentiated (grade I–II) [HR=0.40; 95% CI: 0.20–0.90] patients were more suitable for LTD/LTE, leading to improved OS and CSS outcomes.
Conclusion: It was determined that the long-term outcomes of LTD/LTE are comparable to TH and can serve as a safe option for selected patients with stage IA cervical cancer. Future large prospective studies are required to validate our findings and explore differences in recurrence patterns between the two treatment strategies.
Keywords: cervical cancer, local tumor destruction/excision, total hysterectomy, propensity score matching analysis, SEER database, long-term outcomes

Introduction

Cervical cancer has ascended to become the fourth most prevalent cancer among women globally.[1–3] According to a report by the World Health Organization, in 2022, approximately 660,000 women were diagnosed with cervical cancer, with 350,000 deaths attributed to the disease. Cervical cancer not only jeopardizes the life and health of middle-aged women but also undermines the well-being of their families. Its impact extends beyond individuals,

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imposing substantial economic burdens on households and society.[4] With the widespread dissemination of cervical cancer screening and advancements in screening technologies, there has been a significant decrease in both the incidence and mortality rates of cervical cancer, coupled with an increase in the detection rate of early-stage cervical cancer.[1,4]

With the increasing proportion of early-stage cervical cancer among all cervical cancer cases, there is a growing emphasis on exploring treatment methods that can achieve curative effects while minimizing significant trauma. When early-stage cervical cancer is treated with scientifically appropriate interventions, patients often achieve a satisfactory prognosis and quality of life. According to the guidelines provided by the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO), total hysterectomy(TH) remains the recommended primary treatment modality for early-stage cervical cancer. For patients with stage IA cervical cancer who desire fertility preservation, local tumor destruction/excision (LTD/LTE) is a viable option.[5,6]

Multiple retrospective studies have indicated that for early-stage cervical cancer patients who desire to preserve fertility, LTD/LTE such as cervical conization or radical vaginal trachelectomy may be viable options, potentially demonstrating oncologic outcomes comparable to TH.[7–9] LTD/LTE can serve as a safe option for individuals who desire to retain their uterus, especially for those who are deemed suitable candidates. The prospective study conducted by Kathleen M. Schmeler et al also suggests that conservative surgeries, such as LTD/LTE, are feasible for appropriately selected low-risk early-stage cervical cancer patients.[10] Histological type is a critical factor in evaluating uterine preservation. Early-stage high-risk histological subtypes of cervical cancer are associated with a higher recurrence risk, rendering them unsuitable for uterine preservation surgery.[11–13] Given that TH entails greater trauma compared to LTD/LTE, and advancements in reproductive technologies can meet the fertility needs of older females, an increasing number of early-stage cervical cancer patients are opting for LTD/LTE. However, there remains a lack of comparative long-term outcome studies between LTD/LTE and TH for stage IA cervical cancer. Consequently, there is still controversy over which surgical approach achieves optimal results for such patients. Additionally, the optimal target population for LTD/LTE has yet to be clearly defined. Hence, this study intends to compare the long-term outcomes of LTD/LTE and TH for stage IA cervical cancer. It also aims to identify the optimal target population for LTD/LTE, providing evidence for clinical decision-making and enhancing the quality of survival for patients with stage IA cervical cancer. We hypothesize that the long-term survival outcomes following LTD/LTE are comparable to those following TH in patients with stage IA cervical cancer.

Patients and Methods

Data Source and Patient Selection

The Surveillance, Epidemiology, and End Results (SEER) database (www.seer.cancer.gov) is an open-access resource containing clinical data and patient survival information on various cancers, covering approximately half of all cancer patients in the United States. It encompasses patient demographics, socioeconomic, tumor features, treatment processes, follow-up for vital status, causes of death, and more.[14] The study received ethical approval from the Institutional Review Board of Fujian Cancer Hospital (K2024-210-01). Our research strictly follows the Declaration of Helsinki. Because the SEER database is a database that is free and open to the public, we applied for an informed exemption.

This study is a multicenter retrospective cohort study that conforms to the Strengthening The Reporting of Cohort Studies in Surgery (STROCSS) criteria.[15] The data on a total of 46,545 patients diagnosed with cervical cancer from the SEER database between the years 2004 and 2017 was obtained. Next, we selected patients based on the following inclusion and exclusion criteria. The inclusion criteria were as follows: (1) The FIGO stage of cervical cancer is stage IA, including stage IA1 and stage IA2. The exclusion criteria are: (1) no surgery; (2) two or more malignant tumors; (3) absence of follow-up data or zero follow-up time; (4) less than one-month follow-up. Finally, 6382 patients were enrolled in the study. The flow chart of patient selection is illustrated in Figure 1.

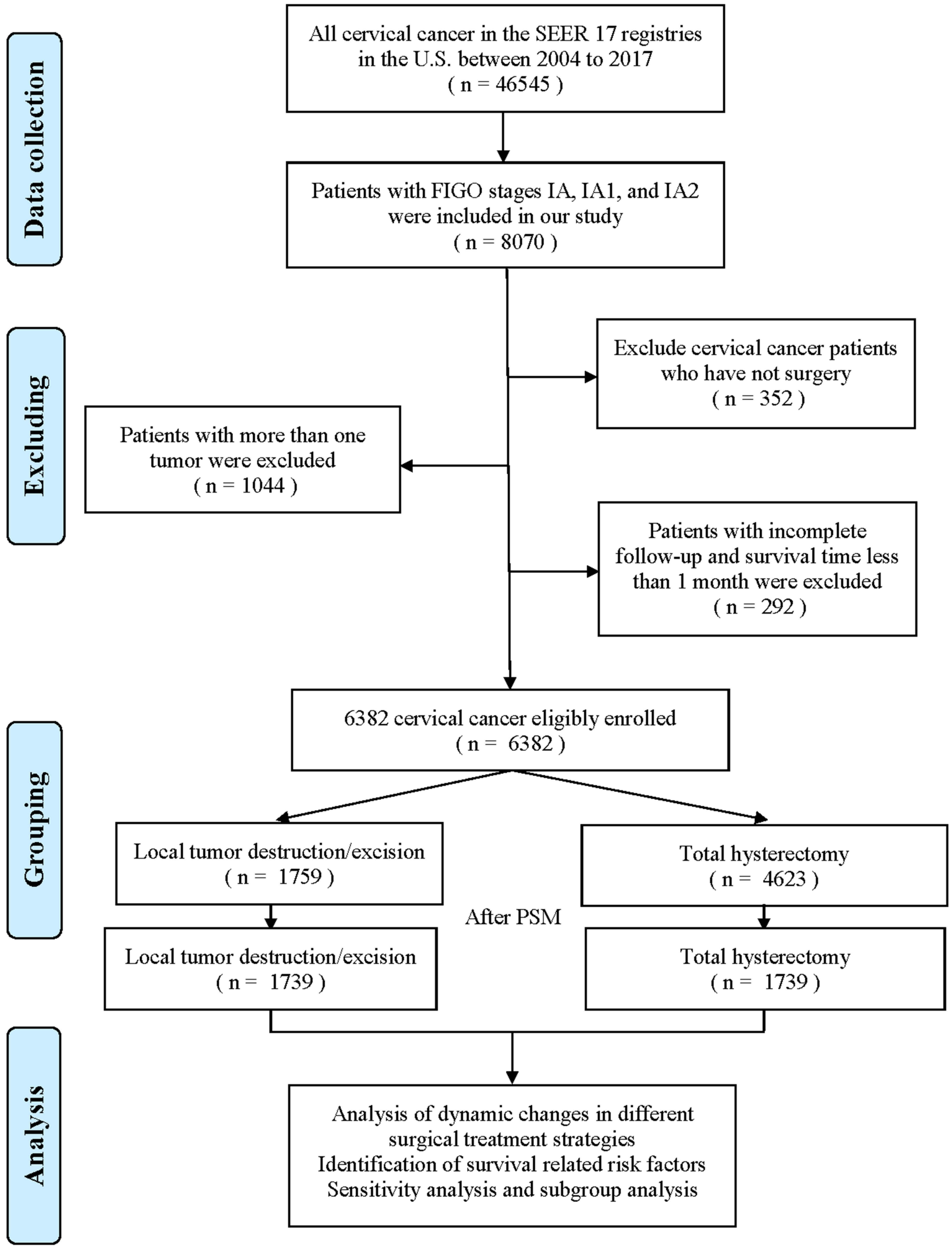

Figure 1 A flow chart illustrating the process of data collection, excluding, grouping, and analysis.

Data Collection and Outcomes

Patient demographics (age, year at diagnosis, marital status at diagnosis, race), socioeconomics, geographic characteristics (origin, residence), tumor features (primary site, tumor size, grade, histology, stage), treatment (time from diagnosis to treatment, radiation, chemotherapy, systemic therapy), follow-up for vital status and causes of death were collected. Based on the different surgical strategies, stage IA cervical cancer was divided into two groups: the local tumor destruction/excision (LTD/LTE) group (codes 20–30) and the total hysterectomy (TH) group (codes 30–90). The surgery codes were proposed by the American College of Surgeons Commission on Cancer Facility Oncology Registry Data System. The primary endpoints of the study are overall survival (the time from diagnosis to death from any cause) and cancer-specific survival (time from diagnosis to death due to cervical cancer) among cervical cancer patients.

Statistical Analysis

Based on the available data, patients were categorized into two groups based on different surgical strategies: the LTD/LTE group and the TH group. Chi-square test or Fisher's exact test was used to compare categorical variables between the two groups. To reduce the influence of confounding factors, 1:1 propensity score matching (PSM) was performed between LTD/LTE group and TH group, with a caliper width set at 0.2. Standardized mean differences< 0.1 were considered to support the assumption of a balance between the groups. The Kaplan-Meier method and the Log- rank test were employed to plot survival curves and compare overall survival (OS) and cancer-specific survival (CSS) between the two groups before and after PSM. Additionally, we employed univariable and multivariable Cox proportional hazard models to identify factors associated with OS and CSS, calculating hazard ratios (HR) and 95% CI. In constructing the multivariable model, we employed a backward stepwise selection method to iteratively exclude non-significant variables ($p \geq 0.05$) to optimize the final model. The Schoenfeld residual test was used to evaluate the proportional hazards assumption of the Cox model. To evaluate the model's goodness of fit, the Akaike Information Criterion (AIC) method was applied, selecting the model with the lowest AIC value as the best fit. Lower AIC values indicate a superior fit to the data.[16,17] This study utilized R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) for all statistical analyses. The R packages Survminer, survival, and MatchIt were used for data analysis. A two-sided P-value < 0.05 was considered statistically significant.

Results

Patient Characteristics

This study ultimately included 6382 stage IA cervical cancer patients. Among them, 1759 individuals (27.6%) underwent LTD/LTE, while 4623 individuals (72.4%) underwent TH. There were 4972 patients (77.9%) aged <50 years old. Younger patients (<50 years) were more likely to undergo LTD/LTE (87.4% vs 74.3%, $p < 0.001$). Additionally, compared to other racial groups, whites had a higher proportion in both the LTD/LTE and TH groups ($p<0.001$). The proportions of larger tumor sizes (≥15mm) ($p < 0.001$) and GX tumors ($p<0.001$) were the lowest in both groups. Compared to patients with stage IA2 cervical cancer, those with stage IA1 were more likely to undergo LTD/LTE (74.0% vs 69.3%, $p < 0.001$). Besides, we observed a higher proportion of patients with a time from diagnosis to treatment of less than 1 month between the two groups ($p < 0.001$). Patients who underwent LTD/LTE were more likely to receive radiation therapy (95.2% vs 96.6%, $p = 0.011$). There were no significant differences between the two groups in terms of the year of diagnosis ($p=0.296$), origin ($p=0.376$), chemotherapy ($p=0.144$), or systemic therapy ($p=0.310$). The detailed baseline characteristics of the patients are shown in Table 1.

We found a significant increase in the proportion of patients with stage IA cervical cancer who underwent LTD/LTE in the years 2005, 2008, 2014, and 2015 compared to previous years (Figure 2A). Simultaneously, from Figure 2B, we observe an overall increasing trend in the proportion of stage IA cervical cancer patients who received LTD/LTE, rising from 26.7% (2004–2008) to 28.8% (2014–2017). Meanwhile, patients of older age (≥50 years) [OR=2.59; 95% CI: 2.20–3.06], those who are married[OR=1.87; 95% CI: 1.65–2.11], those with larger tumor size (≥15mm) [OR=1.35; 95% CI: 1.02–1.80], those with Grade II tumor [OR=1.22; 95% CI: 1.02–1.46], those diagnosed with stage IA2 [OR=1.63; 95% CI: 1.25–2.13], and those experiencing a longer time from diagnosis to treatment [1 month: OR=1.26,95% CI: 1.06–1.50; 2 months: OR=1.93,95% CI: 1.53–2.44; 3+ months: OR=2.07; 95% CI: 1.58–2.70] were more inclined to undergo TH (Supplement Table 1). Conversely, patients from metropolitan areas with populations exceeding 1 million [OR=0.70; 95% CI: 0.54–0.90], those of non-Black or White races [OR=0.82; 95% CI: 0.67–0.99], those with tumors originating from exocervix [OR=0.59; 95% CI: 0.42–0.81], those with histology of squamous cell carcinoma [OR=0.80; 95% CI: 0.68–0.94], and those who received radiation [OR=0.36; 95% CI: 0.27–0.49] were more inclined to undergo LTD/LTE (Supplement Table 1).

Propensity Score Matching

To reduce the impact of confounding factors, we conducted 1:1 PSM between the LTD/LTE group and the TH group, with a caliper width set at 0.2. After PSM, a total of 3478 patients were included in the study, with 1739 patients in both

Table 1 Imbalance of Patient Characteristics Before and After Propensity Score Matching in Stage IA Cervical Cancer Patients

Characteristic	Before PSM			After PSM		
	Local Tumor Destruction/ Excision, N=1759	Total Hysterectomy, N=4623	SMD	Local tumor Destruction/ Excision, N=1739	Total Hysterectomy, N=1739	SMD
Age (years)			0.339			0.059
<50	1538 (87.4%)	3434 (74.3%)		1519 (87.3%)	1484 (85.3%)	
≥50	221 (12.6%)	1189 (25.7%)		220 (12.7%)	255 (14.7%)	
Year of diagnosis			0.042			0.022
2004–2008	620 (35.3%)	1696 (36.7%)		617 (35.5%)	635 (36.5%)	
2009–2013	610 (34.7%)	1625 (35.2%)		604 (34.7%)	591 (34.0%)	
2014–2017	529 (30.1%)	1302 (28.2%)		518 (29.8%)	513 (29.5%)	
Origin recode			0.025			0.011
Spanish-Hispanic-Latino	408 (23.2%)	1122 (24.3%)		404 (23.2%)	412 (23.7%)	
Non-Spanish-Hispanic-Latino	1351 (76.8%)	3501 (75.7%)		1335 (76.8%)	1327 (76.3%)	
Marital status at diagnosis			0.143			0.079
Non-Married	930 (52.9%)	1904 (41.2%)		918 (52.8%)	865 (49.7%)	
Married	677 (38.5%)	2452 (53.0%)		674 (38.8%)	741 (42.6%)	
Unknown	152 (8.6%)	267 (5.8%)		147 (8.5%)	133 (7.7%)	
Median household income inflation			0.107			0.055
<$49,999	143 (8.1%)	542 (11.7%)		143 (8.2%)	163 (9.4%)	
$50,000 - $69,999	754 (42.9%)	1972 (42.7%)		744 (42.8%)	765 (44.0%)	
>$70,000	861 (49.0%)	2109 (45.6%)		852 (49.0%)	811 (46.6%)	
Unknown	1 (0.1%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Rural-Urban Continuum			0.159			0.070
Nonmetropolitan	141 (8.0%)	523 (11.3%)		141 (8.1%)	151 (8.7%)	
Counties in metropolitan areas of lt 250 thousand pop	107 (6.1%)	376 (8.1%)		107 (6.2%)	135 (7.8%)	
Counties in metropolitan areas of 250,000 to 1 million pop	335 (19.0%)	935 (20.2%)		334 (19.2%)	335 (19.3%)	
Counties in metropolitan areas ge 1 million pop	1168 (66.4%)	2785 (60.2%)		1153 (66.3%)	1114 (64.1%)	
Unknown	8 (0.5%)	4 (0.1%)		4 (0.2%)	4 (0.2%)	
Race			0.101			0.044
White	1363 (77.5%)	3697 (80.0%)		1356 (78.0%)	1354 (77.9%)	
Black	161 (9.2%)	449 (9.7%)		159 (9.1%)	170 (9.8%)	
Other	186 (10.6%)	435 (9.4%)		181 (10.4%)	182 (10.5%)	
Unknown	49 (2.8%)	42 (0.9%)		43 (2.5%)	33 (1.9%)	
Primary Site			0.077			0.049
Endocervix	316 (18.0%)	1034 (22.4%)		313 (18.0%)	337 (19.4%)	
Exocervix	88 (5.0%)	135 (2.9%)		85 (4.9%)	73 (4.2%)	
Overlapping lesion of cervix uteri	25 (1.4%)	84 (1.8%)		25 (1.4%)	28 (1.6%)	
Cervix uteri	1330 (75.6%)	3370 (72.9%)		1316 (75.7%)	1301 (74.8%)	
Tumor size (mm)			0.173			0.091
<15	738 (42/0%)	2253 (48.7%)		733 (42.1%)	797 (45.8%)	
≥15	74 (4.2%)	339 (7.3%)		67 (3.9%)	80 (4.6%)	
Unknown	947 (53.8%)	2031 (43.9%)		939 (54.0%)	862 (49.6%)	
Grade			0.238			0.123
Well differentiated; Grade I	337 (19.2%)	1018 (22.0%)		334 (19.2%)	350 (20.1%)	
Moderately differentiated; Grade II	335 (19.0%)	1220 (26.4%)		332 (19.1%)	397 (22.8%)	
Poorly differentiated; Grade III	107 (6.1%)	432 (9.3%)		106 (6.1%)	122 (7.0%)	
Undifferentiated; anaplastic; Grade IV	17 (1.0%)	45 (1.0%)		17 (1.0%)	11 (0.6%)	
Unknown	963 (54.8%)	1908 (41.3%)		950 (54.6%)	859 (49.4%)	
Histology recode			0.155			0.050
Adenocarcinoma	375 (21.3%)	1325 (28.7%)		373 (21.5%)	406 (23.4%)	
Squamous cell carcinoma	1289 (73.3%)	3074 (66.5%)		1271 (73.1%)	1232 (70.9%)	
Others	95 (5.4%)	224 (4.9%)		95 (5.5%)	101 (5.8%)	

(*Continued*)

Table 1 (Continued).

Characteristic	Before PSM			After PSM		
	Local Tumor Destruction/ Excision, N=1759	Total Hysterectomy, N=4623	SMD	Local tumor Destruction/ Excision, N=1739	Total Hysterectomy, N=1739	SMD
FIGO stage			0.15			0.074
IA	121 (6.9%)	252 (5.5%)		118 (6.8%)	111 (6.4%)	
IA1	1302 (74.0%)	3202 (69.3%)		1287 (74.0%)	1242 (71.4%)	
IA2	336 (19.1%)	1169 (25.3%)		334 (19.2%)	386 (22.2%)	
Months from diagnosis to treatment			0.268			0.102
0	1361 (77.4%)	3036 (65.7%)		1344 (77.3%)	1280 (73.6%)	
1	221 (12.6%)	749 (16.20%)		221 (12.7%)	231 (13.28%)	
2	103 (5.9%)	476 (10.30%)		100 (5.8%)	131 (7.53%)	
3+	73 (4.2%)	358 (7.74%)		73 (4.2%)	96 (5.52%)	
Unknown	1 (0.1%)	4 (0.09%)		1 (0.1%)	1 (0.06%)	
Radiation			0.07			0.021
No	1674 (95.2%)	4464 (96.56%)		1659 (95.4%)	1651 (94.94%)	
Yes	85 (4.8%)	159 (3.44%)		80 (4.6%)	88 (5.06%)	
Chemotherapy			0.041			<0.001
No/Unknown	1714 (97.4%)	4533 (98.05%)		1698 (97.6%)	1698 (97.64%)	
Yes	45 (2.6%)	90 (1.95%)		41 (2.4%)	41 (2.36%)	
Systemic therapy			0.011			0.017
No	1351 (76.8%)	3542 (76.62%)		1335 (76.8%)	1323 (76.08%)	
Yes	40 (2.3%)	80 (1.73%)		37 (2.1%)	37 (2.13%)	
Unknown	368 (20.9%)	1001 (21.65%)		367 (21.1%)	379 (21.79%)	

Notes: SMD < 0.1 was considered to support the assumption of a balance between the groups.
Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; PSM, Propensity score matching; SMD, standardized mean differences.

the LTD/LTE group and the TH group. Two groups after PSM have excellent matching outcomes (Supplement Figure 1). Most of the standardized mean differences for baseline characteristics between the two groups were below 0.1 (Supplement Figure 2). After PSM, the detailed baseline characteristics of patients in both groups are exhibited in Table 1. Following PSM, we acquired matched cohorts with closely aligned baseline characteristics in both groups.

Survival Analyses of LTD/LTE and TH

Before and after PSM, we conducted survival analysis on the LTD/LTE and TH groups, respectively. Before PSM, there were no significant differences in OS (P=0.520) and CSS (P=0.380) between the LTD/LTE and TH groups (Figure 3A and B). After PSM, a significant difference was observed in OS (P=0.030) between the two groups, while no significant difference was observed in CSS (P=0.110) (Figure 4A and B). Additionally, within the stage IA1 (OS:P=0.018, CSS: P=0.230; Figure 5) and stage IA2 (OS:P=0.071, CSS:P=0.240; Figure 6) subgroups, there were no significant differences observed in survival analyses between the two groups.

Prognostic Factors of Survival

Before PSM, the univariable Cox proportional hazards regression analysis indicated that age, marital status at diagnosis, median household income, race, tumor size, tumor grade, histology, stage, radiation, chemotherapy, and systemic therapy were closely associated with OS in patients with stage IA cervical cancer. Age, marital status at diagnosis, race, tumor size, tumor grade, time from diagnosis to treatment, stage, radiation, chemotherapy, and systemic therapy were found to be associated with patients' CSS (Supplement Table 2). In the multivariable cox proportional hazards regression analysis, the results revealed that older age (≥50 years) [HR=1.06; 95% CI: 1.06–1.07], blacks [HR=1.46; 95% CI: 1.08–1.96], grade III [HR=1.92; 95% CI: 0.71–1.53], squamous cell carcinoma [HR=1.53; 95% CI: 1.11–2.10], radiation [HR=2.13; 95% CI: (1.40–3.23)] and chemotherapy [HR=2.80; 95% CI: 1.25–6.27] were independently associated with poorer OS. Conversely, being married [HR=0.67; 95% CI: 0.53–0.85] was independently associated with better OS. And we

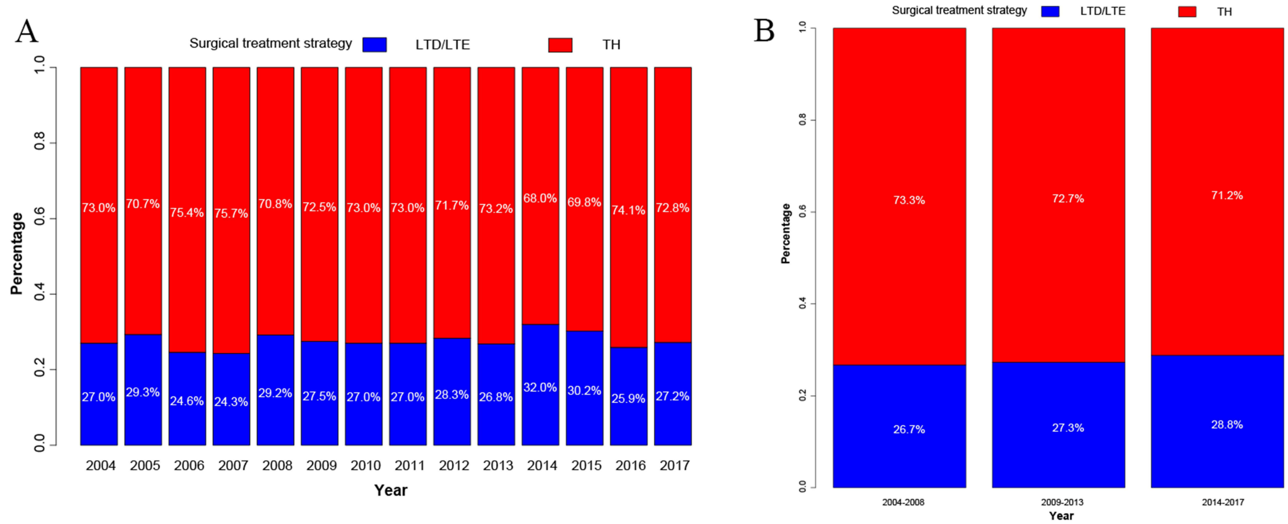

Figure 2 The proportion of patients with stage IA cervical cancer undergoing different treatment strategies every year (**A**) or every 5 years (**B**) between 2004 and 2017.

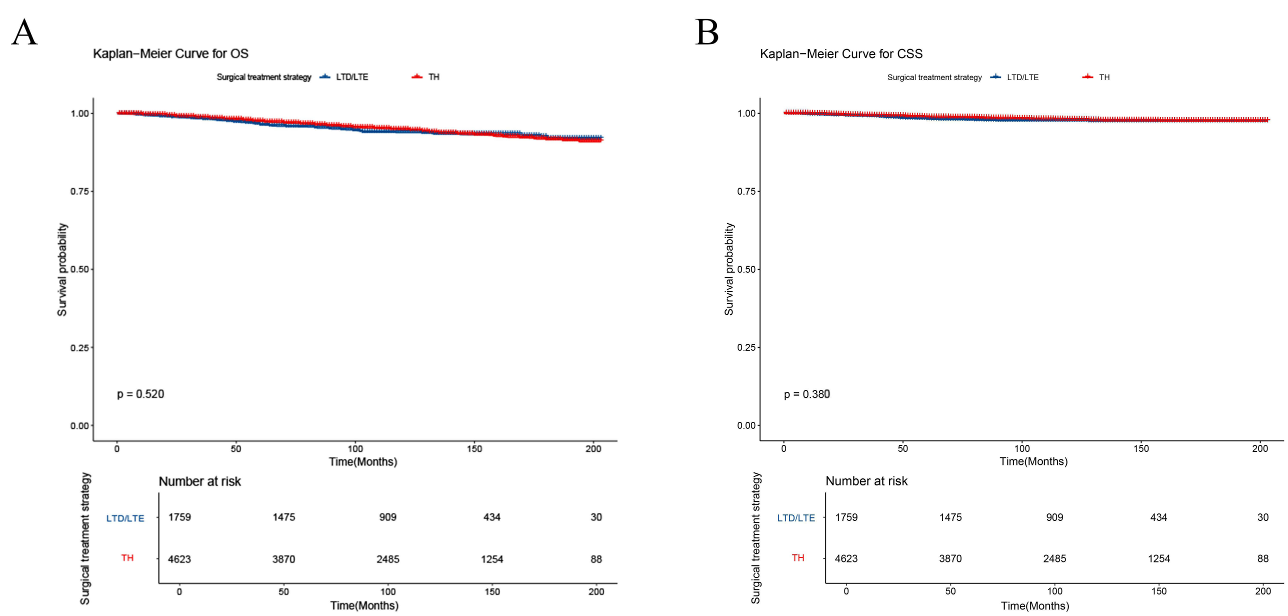

Figure 3 Kaplan-Meier curve of OS(**A**) and CSS(**B**) in patients with stage IA cervical cancer before propensity score matching(PSM).
Abbreviations: OS, overall survival; CSS, cancer-specific survival.

observed that older age (≥50 years) [HR=1.04; 95% CI: 1.02–1.05], larger tumor size (≥15mm) [HR=1.93; 95% CI: 1.13–3.30], grade III [HR=3.46; 95% CI: 1.78–6.73], a slightly longer time from diagnosis to treatment (≥1 month but<2 months) [HR=1.71; 95% CI: 1.09–2.69], radiation [HR=2.65; 95% CI: 1.41–4.98], and chemotherapy [HR=5.34; 95% CI: 1.99–14.39] were independent factors related with poorer CSS, while being married [HR=0.60; 95% CI: 0.40–0.89] and stage IA1 [HR=0.49; 95% CI: 0.26–0.93] were independent factors related with better CSS (Supplement Table 2). The effects of relevant detailed factors on OS and CSS are summarized in Supplement Table 1. It is noteworthy that surgical treatment strategy showed no significant relationship with either OS (p=0.524) or CSS (p=0.382) in patients.

The results of Cox proportional hazards regression analysis after PSM are displayed in Table 2. Age, median household income, race, tumor size, grade, therapeutic method, histology, stage, time from diagnosis to treatment, radiation, chemotherapy, and systemic therapy were found to be associated with OS in patients with stage IA cervical cancer. Similarly, age, median household income, tumor size, grade, stage, time from diagnosis to treatment, radiation,

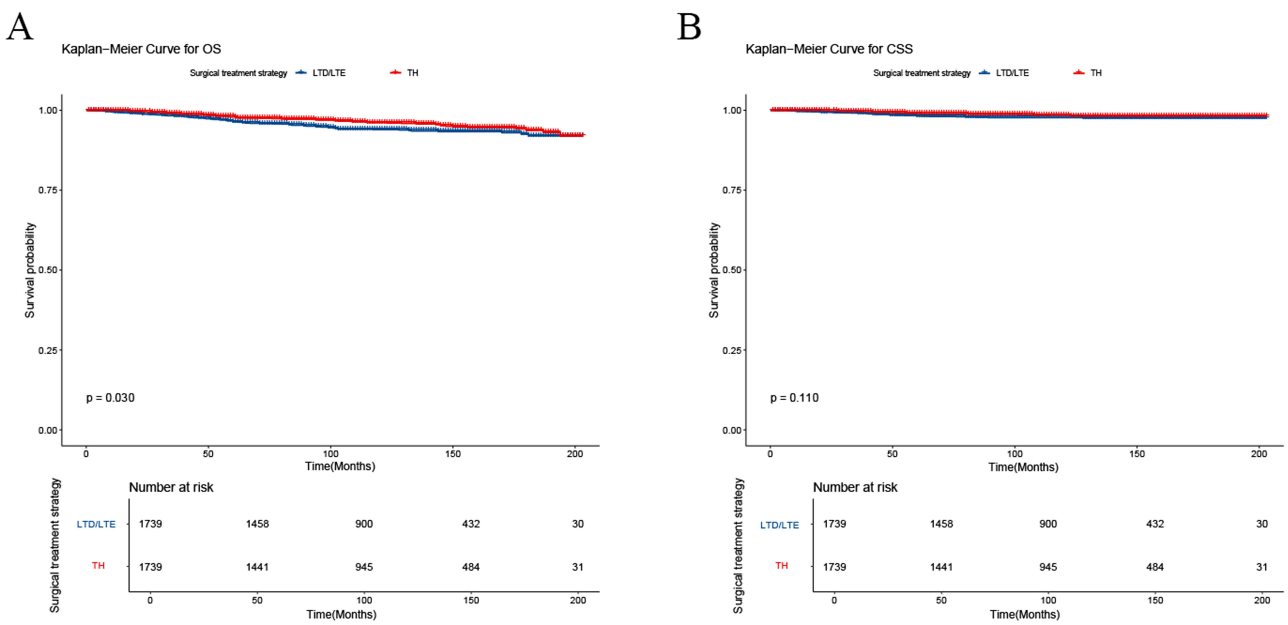

Figure 4 Kaplan-Meier curve of OS(**A**) and CSS(**B**) in patients with stage IA cervical cancer after propensity score matching(PSM).
Abbreviations: OS, overall survival; CSS, cancer-specific survival.

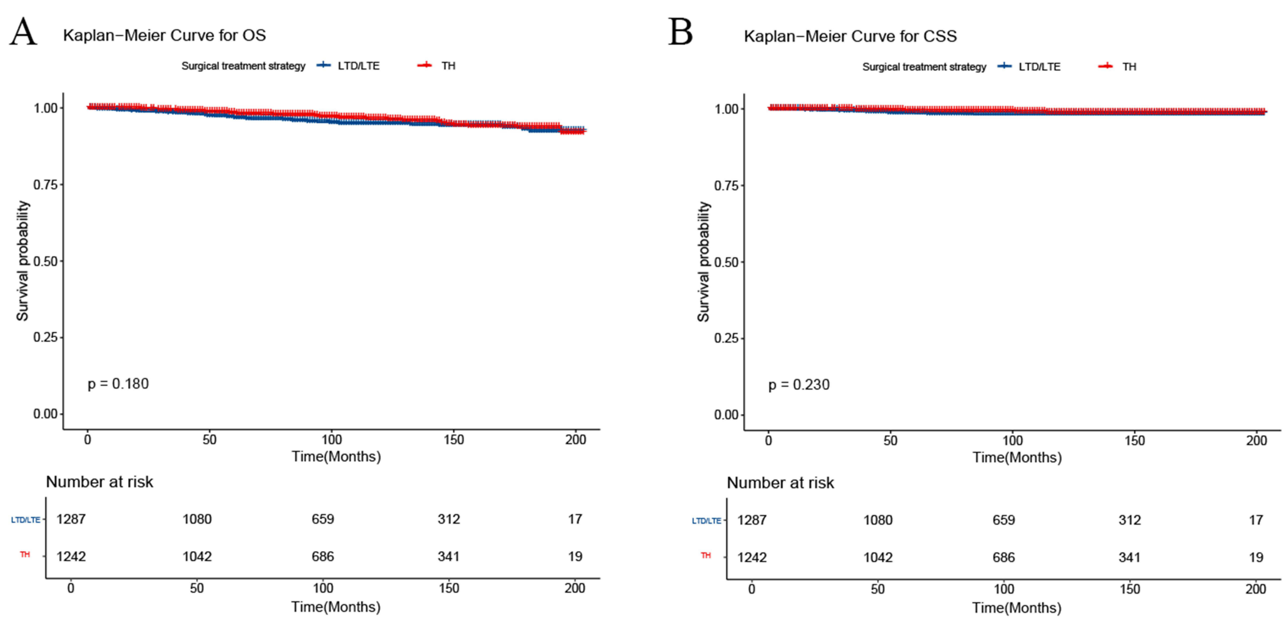

Figure 5 Kaplan-Meier curve of OS(**A**) and CSS(**B**) in patients with stage IA1 cervical cancer after propensity score matching(PSM).
Abbreviations: OS, overall survival; CSS, cancer-specific survival.

chemotherapy, and systemic therapy were related to CSS in patients. In the multivariable regression analysis, older age (≥50 years)[OS: HR=4.13, 95%CI: 2.91–5.85; CSS: HR=1.05, 95% CI: 1.03–1.07] and radiation [OS:HR=3.02, 95%CI: 1.78–5.14; CSS: HR=3.36,95%CI: 1.49–7.58] were identified as the risk factors associated with decreased OS and CSS. Conversely, higher household income (>$70,000) [HR=0.45; 95% CI: 0.28–0.75] and total hysterectomy [HR=0.67; 95% CI: 0.49–0.94] were identified as risk factors associated with improved OS. Notably, while TH was found to be associated with improved OS, no significant relationship was observed between TH and CSS (P=0.116).

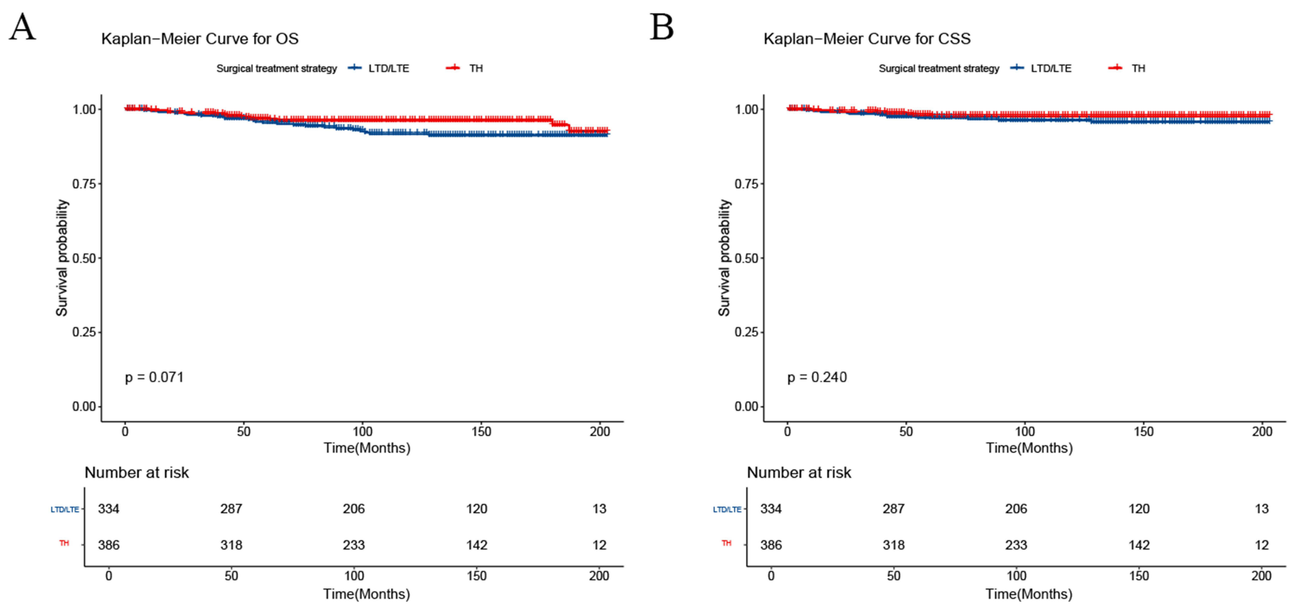

Figure 6 Kaplan-Meier curve of OS(**A**) and CSS(**B**) in patients with stage IA2 cervical cancer after propensity score matching(PSM).
Abbreviations: OS, overall survival; CSS, cancer-specific survival.

Subgroup Analysis of Survival Outcomes

By comparing the outcomes of different surgical treatment strategies across subsets defined by various baseline variables, it was observed that in certain specific subgroups, patients undergoing TH or LTD/LTE had the potential to achieve better survival outcomes. Patients with the following characteristics tend to achieve better OS when undergoing TH: age≥50 years [HR=2.20; 95% CI: 2.20–3.30], overlapping lesion of cervix uteri as the primary tumor site [HR=6.00; 95% CI:1.10–32.10],

Table 2 The Univariable and Multivariable Cox Regression Analysis of OS and CSS in Stage IA Cervical Cancer Patients After PSM

Characteristic	OS		CSS	
	Univariable Analysis	Multivariable Analysis	Univariable Analysis	Multivariable Analysis
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Age (years)				
<50	Reference	Reference	Reference	Reference
≥50	5.88 (4.28–8.08)	4.13(2.91–5.85)	3.52 (2.05–6.05)	1.05(1.03–1.07)
Year of diagnosis				
2004–2008	Reference		Reference	
2009–2013	1.02 (0.70–1.48)		1.07 (0.60–1.91)	
2014–2017	1.16 (0.72–1.87)		1.03 (0.50–2.11)	
Origin recode				
Spanish-Hispanic-Latino	Reference		Reference	
Non-Spanish-Hispanic-Latino	1.29 (0.85–1.97)		0.93 (0.50–1.73)	
Marital status at diagnosis				
Non-Married	Reference		Reference	
Married	0.71 (0.50–1.00)		0.76 (0.43–1.33)	
Unknown	1.13 (0.65–1.95)		1.22 (0.51–2.91)	
Median household income inflation				
< $49,999	Reference	Reference	Reference	Reference
$50,000 - $69,999	0.66 (0.41–1.07)	0.77(0.46–1.27)	0.66 (0.32–1.39)	0.87(0.40–1.86)
> $70,000	0.45 (0.28–0.75)	0.57(0.34–0.96)	0.34 (0.15–0.76)	0.47(0.20–1.08)

(*Continued*)

Table 2 (Continued).

Characteristic	OS		CSS	
	Univariable Analysis	Multivariable Analysis	Univariable Analysis	Multivariable Analysis
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Rural-Urban Continuum				
Nonmetropolitan	Reference		Reference	
Counties in metropolitan areas of lt 250 thousand pop	1.62 (0.75–3.50)		2.27 (0.68–7.55)	
Counties in metropolitan areas of 250,000 to 1 million pop	1.41 (0.72–2.77)		1.48 (0.49–4.48)	
Counties in metropolitan areas ge 1 million pop	1.03 (0.55–1.92)		1.00 (0.35–2.82)	
Unknown	0 (0-Inf)		0 (0-Inf)	
Race				
White	Reference	Reference	Reference	
Black	1.56 (1.01–2.42)	1.26(0.80–1.99)	1.41 (0.66–2.99)	
Other	0.67 (0.36–1.24)	0.69(0.37–1.30)	0.80 (0.32–2.01)	
Unknown	0 (0-Inf)	0 (0-Inf)	0 (0-Inf)	
Primary Site				
Endocervix	Reference		Reference	
Exocervix	0.94 (0.39–2.27)		1.67 (0.52–5.31)	
Overlapping lesion of cervix uteri	2.05 (0.79–5.34)		2.30 (0.50–10.50)	
Cervix uteri	1.14 (0.75–1.75)		1.07 (0.54–2.14)	
Tumor size (mm)				
<15	Reference	Reference	Reference	Reference
≥15	2.31 (1.30–4.12)	1.18(0.62–2.25)	4.53 (2.08–9.90)	1.76(0.72–4.28)
Unknown	0.90 (0.65–1.26)	0.79(0.56–1.12)	1.06 (0.60–1.86)	0.98(0.55–1.77)
Grade				
Well differentiated; Grade I	Reference	Reference	Reference	Reference
Moderately differentiated; Grade II	1.69 (0.98–2.91)	1.27(0.72–2.21)	2.31 (1.02–5.25)	1.58(0.68–3.68)
Poorly differentiated; Grade III	2.85 (1.53–5.29)	1.81(0.94–3.48)	3.79 (1.50–9.61)	2.08(0.80–5.44)
Undifferentiated; anaplastic; Grade IV	0.90 (0.12–6.68)	0.73(0.10–5.62)	0 (0-Inf)	0 (0-Inf)
Unknown	1.20 (0.73–1.96)	1.33(0.79–2.23)	0.86 (0.38–1.96)	1.12(0.48–2.61)
Therapeutic method				
Local tumor destruction/excision	Reference	Reference	Reference	
Total hysterectomy	0.70 (0.51–0.97)	0.67(0.49–0.94)	0.66 (0.39–1.11)	
Histology recode				
Adenocarcinoma	Reference	Reference	Reference	
Squamous cell carcinoma	1.55 (1.00–2.41)	1.54(0.96–2.47)	1.45 (0.73–2.87)	
Others	0.71 (0.27–1.87)	0.57(0.21–1.57)	0.38 (0.05–2.94)	
FIGO stage				
IA	Reference	Reference	Reference	Reference
IA1	0.52 (0.29–0.93)	0.77(0.40–1.45)	0.34 (0.15–0.78)	0.63(0.25–1.58)
IA2	0.64 (0.34–1.21)	0.66(0.34–1.31)	0.75 (0.32–1.78)	0.80(0.31–2.08)
Months from diagnosis to treatment				
0	Reference	Reference	Reference	Reference
1	1.46 (0.95–2.25)	1.49(0.96–2.33)	2.07 (1.10–3.89)	1.88(0.98–3.63)
2	1.31 (0.71–2.44)	1.00(0.52–1.90)	1.65 (0.65–4.19)	1.09(0.41–2.87)
3+	1.83 (1.01–3.32)	1.57(0.85–2.89)	1.30 (0.40–4.22)	1.19(0.36–3.95)
Unknown	0 (0-Inf)	0 (0-Inf)	0 (0-Inf)	0 (0-Inf)
Radiation				
No	Reference	Reference	Reference	Reference
Yes	7.35 (5.09–10.60)	3.02(1.78–5.14)	11.29 (6.57–19.41)	3.36(1.49–7.58)
Chemotherapy				
No/Unknown	Reference	Reference	Reference	Reference
Yes	6.81 (4.16–11.15)	2.43(0.77–7.64)	11.15 (5.78–21.52)	2.47(0.49–12.39)

(*Continued*)

Table 2 (Continued).

Characteristic	OS		CSS	
	Univariable Analysis	Multivariable Analysis	Univariable Analysis	Multivariable Analysis
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Systemic therapy				
No	Reference	Reference	Reference	Reference
Yes	6.07 (3.46–10.64)	0.57(0.16–1.97)	10.25 (4.92–21.33)	0.62(0.11–3.46)
Unknown	0.95 (0.65–1.40)	0.97(0.64–1.46)	1.13 (0.60–2.11)	1.07(0.54–2.11)

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; PSM, Propensity score matching; OS, Overall survival; CSS, Cancer-specific survival; HR, Hazard Ratio; 95% CI, 95% Confidence Interval.

histology other than squamous cell carcinoma and usual-type adenocarcinoma [HR=4.40; 95% CI: 1.80–11.10], or receiving systemic therapy [HR=2.40; 95% CI: 1.00–5.70]. Patients with Grade II tumors [HR=0.40; 95% CI: 0.20–0.70] or individuals who have received radiation [HR=0.40; 95% CI: 0.20–0.70] tend to achieve better OS when undergoing LTD/LTE (Figure 7). For CSS, patients aged≥50 years [HR=2.30; 95% CI:1.10–4.90] tend to have better CSS when undergoing TH; patients with Grade II tumors [HR=0.40; 95% CI:0.20–0.90] are more suitable for undergoing LTD/LTE, with the potential for better CSS (Figure 7). In the remaining subgroups, TH and LTD/LTE demonstrate similar OS and CSS, as depicted in Figure 7.

Discussion

The current primary surgical treatment strategy for stage IA cervical cancer remains radical hysterectomy. However, a substantial proportion of patients diagnosed with stage IA cervical cancer are young individuals.[18] Most young patients express a strong desire to retain their uterus, and some elderly patients also cling to this desire due to traditional beliefs. The most significant consequence of uterine removal for young patients is infertility. Infertility can trigger a cascade of

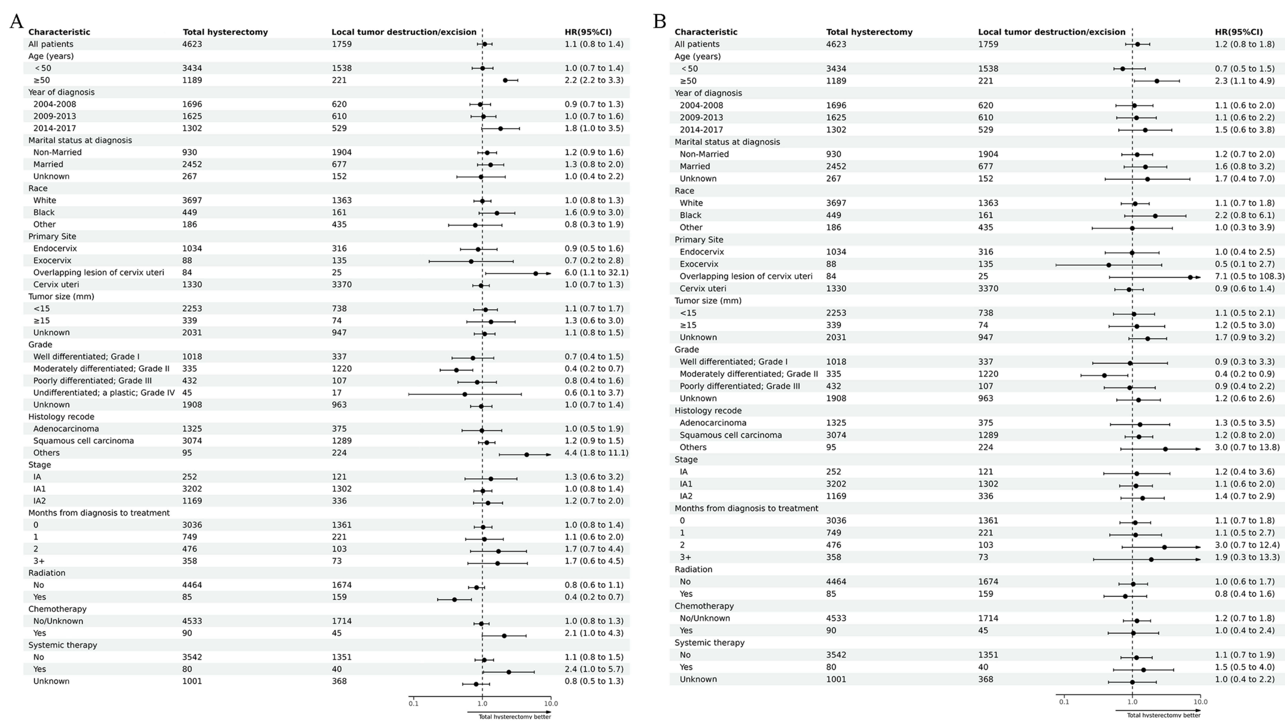

Figure 7 The Forest plots of subgroup analysis for OS(**A**) and CSS(**B**) according to the surgery strategies.
Abbreviations: OS, overall survival; CSS, cancer-specific survival.

effects, potentially increasing the risk of depression and unhappiness within the family, and ultimately reducing the patient's quality of life.[19] For elderly patients, some have strong and stubborn desires to retain their uterus. Some elderly patients may be unable to tolerate TH due to poor health. Previous studies have also confirmed that LTD/LTE like cervical conization and trachelectomy, have excellent oncological outcomes in selected patients with early-stage cervical cancer.[20–23] This provides insight into whether less radical surgeries, such as LTD/LTE, can be extended to suitable target populations in cases where the risk of recurrence is comparable. The study utilized the SEER database to compare the long-term survival outcomes of LTD/LTE and TH in patients with stage IA cervical cancer. Although OS with TH is superior to that with LTD/LTE, there is no significant difference in oncological outcomes between the two. Therefore, less radical surgeries such as LTD/LTE may be appropriately promoted in suitable patient populations. Besides patients with a strong desire to retain their uterus, young patients with low-risk histological types (squamous cell carcinoma or usual-type adenocarcinoma) and high tissue differentiation (Grade I–II) may constitute the target population for LTD/LTE.

Our results indicated no significant difference in OS and CSS between the LTD/LTE group and the TH group before PSM. This suggests that among stage IA cervical cancer patients, there were no significant differences in the long-term survival outcomes between the two distinct surgical treatment strategies. However, given the significant differences in baseline characteristics between the two groups, the conclusion of comparable long-term survival outcomes between the two different surgical treatment strategies is somewhat controversial. To mitigate the confounding effects, 1:1 PSM was performed on the two groups, resulting in two cohorts with similar baseline characteristics. Surprisingly, subsequent survival analysis revealed that although TH showed a slight advantage over LTD/LTE in terms of OS, there was no significant difference between the two groups in terms of CSS. This provides us with significant inspiration that LTD/LTE may be feasible for specific patients with stage IA cervical cancer. In a prospective study, the residual tumor rate after cervical conization was only 2.5%;[10] Furthermore, in another study involving 50 early-stage low-risk cervical cancer patients, only 4 patients had positive lymph nodes.[24] Therefore, one has to wonder whether radical surgeries may constitute overtreatment in specific early-stage cervical cancer patients. The OS of TH is slightly higher than that of LTD/LTE, while the CSS is similar to that of LTD/LTE, suggesting that the non-tumor-related mortality rate of TH is more favorable compared to LTD/LTE. The difference in OS may be attributed to imperfect matching of non-tumor-related deaths between the two groups, influenced by various confounding factors. For instance, LTD/LTE patients may have potentially higher suicide rates, while TH patients may experience higher follow-up frequency. Importantly, in the IA1 and IA2 subgroups, neither OS nor CSS differed significantly between the two surgical treatment strategies. This suggests that TH should not be regarded as the standard recommended surgical treatment strategy for all IA1 and IA2 cervical cancer patients. Instead, appropriate IA-stage cervical cancer patients should be recommended to undergo LTD/LTE, aligning with the findings of Tommy Buchanan MD et al.[25] It is worth mentioning that although CSS of TH and LTD/LTE are similar, the local recurrence rates and patterns of recurrence in patients undergoing these two surgical treatment strategies remain unclear.[20] In summary, the tumor outcomes between the two surgical treatment strategies are similar and LTD/LTE emerges as a safe option for eligible patients with stage IA cervical cancer. Nevertheless, the recurrence rates and patterns of the two treatment modalities remain unclear and necessitate further exploration in large-scale prospective studies.

Over the past two decades, there has been a gradual increase in the number of stage IA cervical cancer patients opting for LTD/LTE. This trend reflects a growing desire among early-stage cervical cancer patients to retain their uterus. Considering the safety and effectiveness of LTD/LTE, there is growing anticipation for its expanded use in stage IA cervical cancer patients. This raises the question: who are the appropriate candidates for LTD/LTE? Our study identified young patients with low-risk histological types (squamous cell carcinoma or usual-type adenocarcinoma) and well-differentiated tumors (Grade I–II) as potential candidates for LTD/LTE. It is currently believed that the incidence of parametrial invasion and lymph node metastasis of stage IA cervical cancer is very low.[26–29] However, not all patients with stage IA cervical cancer are suitable candidates for LTD/LTE and only specific patients are recommended to undergo less radical surgery. Our study found that older patients tended to have better OS and CSS when receiving TH compared to those undergoing LTD/LTE. Patients undergoing LTD/LTE often require more frequent follow-up due to the possibility of reinfection with human papillomavirus or prevention of uterine-related disease. Most elderly patients are less likely to attend regular follow-up appointments and are more resistant to regular check-ups than younger patients.[30] Furthermore, advanced age has been identified as a major adverse prognostic factor for cervical cancer. Elderly patients exhibit higher mortality rates in cervical cancer, irrespective of comorbidities, histology, or FIGO stage.[30] Therefore, TH may not necessarily be considered overtreatment in older patients. We recommend LTD/LTE for younger patients and TH for older patients. In our study, patients with histology other than squamous cell carcinoma and usual-type adenocarcinoma demonstrated better OS when they underwent TH. Patients with well-differentiated tumors (grade I, grade II) were deemed more suitable for LTD/LTE, potentially resulting in improved OS and CSS. Rare pathological types of cervical cancer, such as neuroendocrine carcinoma and gastric-type cervical adenocarcinoma, display significant biological distinctions from cervical squamous cell carcinoma and usual-type adenocarcinoma. They are characterized by greater invasiveness and a propensity for distant metastasis.[31,32] Currently, total hysterectomy is universally recognized as the preferred treatment strategy for operable patients with these rare pathological types of tumors.[31,33] Moreover, low-grade cervical cancers with more aggressive characteristics also tend to favor radical surgery as their primary treatment modality.

Admittedly, our study has some limitations. Firstly, incomplete data in the SEER database prevented a comparison of recurrence rates and patterns between the two surgical treatment strategies. Further investigation through large-scale prospective studies is warranted. Secondly, missing information on individual baseline characteristics for some patients may have affected the reliability of our findings. Moreover, as a retrospective study, our work is inherently limited by its design. While PSM was employed to mitigate the impact of confounding factors, there remain some variables that could not be perfectly matched, which may have introduced residual confounding in our findings. Additionally, our study excluded patients with no follow-up data or zero follow-up time, which may have introduced survivor bias.

While retrospective studies inherently have limitations, our study is a population-based analysis utilizing extensive data from multiple centers, thereby ensuring the reliability of our findings. Furthermore, we implemented PSM to establish two cohorts with comparable baseline characteristics, mitigating the impact of confounding variables and enhancing the reliability of our findings. Moreover, our study represents the first investigation into the target population eligible for LTD/LTE, offering valuable insights to clinicians for making more cost-effective clinical decisions.

Conclusion

In this study, it was determined that the long-term outcomes of LTD/LTE are comparable to TH, indicating its viability as a safe surgical treatment approach for specific stage IA cervical cancer patients. Young patients diagnosed with low-risk histological types (squamous cell carcinoma or usual-type adenocarcinoma) and well-differentiated (grade I–II) stage IA cervical cancer, may constitute the most suitable demographic for LTD/LTE intervention. Future large-scale prospective studies will be required to validate our findings and investigate potential differences in recurrence patterns between LTD/LTE and TH. Currently, we contend that clinicians may consider recommending LTD/LTE for eligible patients in routine clinical practice, taking into account their preferences and desires.

Data Sharing Statement

Data for this study can be obtained from the SEER database or by emailing the corresponding author. Code and other materials are available on request from the authors.

Ethics Approval and Consent to Participate

This study is a retrospective cohort study of tumor patients based on the US SEER database. Because it is open to everyone and we completed this study in compliance with the Declaration of Helsinki, informed consent and ethical approval were waived.

Consent for Publication

This manuscript has not been published or presented elsewhere in part or entirety and is not under consideration by another journal.

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Author Contributions

All authors read and approved the final manuscript. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there were no potential conflicts of interest in this research.

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