Clinicopathological characteristics and prognostic factors of cervical adenocarcinoma

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We aimed to assess the clinicopathological features and to determine the prognostic factors of cervical adenocarcinoma (AC). Relevant data were extracted from surveillance, epidemiology and end results database from 2004 to 2015. The log-rank test and Cox proportional hazard analysis were subsequently utilized to identify independent prognostic factors. A total of 3102 patients were identified. The enrolled patients were characterized by higher proportion of early FIGO stage (stage I: 65.9%; stage II: 14.1%), low pathological grade (grade I/II: 49.1%) and tumor size ≤ 4 cm (46.8%). The 5- and 10-year cancer-specific survival rates of these patients were 74.47% and 70.00%, respectively. Meanwhile, the 5- and 10-year overall survival (OS) rates were 71.52% and 65.17%, respectively. Multivariate analysis revealed that married status, surgery as well as chemotherapy were independent favorable prognostic indicators. Additionally, aged > 45, tumor grade III/IV, tumor size > 4 cm, advanced FIGO stage and pelvic lymph node metastasis (LNM) were unfavorable prognostic factors (all \(P < 0.01\)). Stratified analysis found that patients without surgery could significantly benefit from chemotherapy and radiotherapy. In addition, chemotherapy could significantly improve the survival in stage II–IV patients and radiotherapy could only improve the survival in stage III patients (all \(P < 0.01\)). Marital status, age, grade, tumor size, FIGO stage, surgery, pelvic LNM and chemotherapy were significantly associated with the prognosis of cervical AC.

Uterine cervix carcinoma is a threatening cause of cancer-related death in females, which is reported to have approximately 311,000 death cases and 570,000 new cases in 2018. Squamous cell carcinoma (SCC) is the most prevalent histological type of cervical cancer and approximately 10–25% of cervical cancer is adenocarcinoma (AC). Additionally, the prevalence of cervical AC has been reported to increase in multiple regions, the proportion of which has been demonstrated to double in the last decade. However, the knowledge of cervical AC is currently limited to small case series, with unclear clinicopathological features and standard treatment. The standard therapeutic regimen of cervical AC is currently the same as SCC, which includes radical hysterectomy along with adjuvant radiotherapy (RT), radical hysterectomy or primary RT for early-stage cancer. In addition, concurrent chemoradiotherapy (CCRT) is prevalently recommended and promoted for locally advancedcancer as well as early-stage FIGO lesions, which gives rise to equivalent outcomes. Nevertheless, cervical SCC and AC patients even with the same Federation International of Gynecology and Obstetrics (FIGO) stage still have disparate prognostic outcomes. At present, whether the standard therapeutic regimen is equally suitable for SCC and AC patients has been doubted due to poorer prognostic outcomes of AC patients than SCC. Therefore, in order to provide a better theoretical therapeutic basis for cervical AC, it is necessary to further understand the survival and prognosis of cervical AC patients. Although some previous studies have demonstrated that FIGO stage, nodal status, tumor size, age and tumor grade were prognostic factors of cervical AC, however, the numbers of patients enrolled in these studies were small, and with inconsistent results. Therefore, it is significant to examine the prognostic indicators for cervical AC based on a large population, aiming at establishing a framework for new therapeutic strategies.

The NCI-supported Surveillance, Epidemiology and End Results (SEER) database, the most authoritative and largest cancer dataset in North America, reports tumor data on approximately 30% of the US population by selecting relevant registries to represent population diversity. Therefore, SEER is a valuable database to investigate such rare tumors. Therefore, a retrospective study was conducted by collecting eligible patients...
from SEER database, aiming at summarizing clinical features, survival and treatment for patients with cervical AC to delineate prognostic factors.

Materials and methods

Ethics statement. It was a population-based retrospective study using SEER database. To acquire relevant data from the database, we signed the SEER Research Data Agreement (No.19817-Nov2018) and further searched for data based on the approved guidelines. All extracted data were publicly accessible and de-identified, and data analysis was considered to be non-human subjects by Office for Human Research Protection. Thus, no approval was requested by the institutional review board.

Study population. SEER*State v8.3.6 (released on August 8, 2019) was utilized to select and identify qualified subjects, which includes 18 SEER regions from 2004 to 2015 (2018 submission). The inclusion criteria were as follows: (1) primary cervical AC patients; (2) the diagnosis of cervical AC was based on ICD-O-3; coded as 8140–849019, 20. Patients were eliminated if they had: (1) more than one primary malignancies; (2) reported diagnosis source from autopsy or death certificate or without pathological diagnosis; (3) without certain necessary clinicopathological data, including surgical style as well as FIGO stage; (4) without prognostic information. The rest of subjects were enrolled as the initial cohort of SEER.

Covariates and endpoint. The following clinicopathological parameters were analyzed: year of diagnosis (2004–2007, 2008–2011, 2012–2015)21; marital status (unmarried, married); race (black, white or others); insured status (uninsured/unknown, any medicaid/insured); age (≤ 45, > 45); grade (grade I/II, grade III/IV, unknown); FIGO stage (stage I, II, III, IV); tumor size (≤ 4 cm, > 4 cm, unknown); pelvic lymph node (LN) dissections (none or biopsy, removal of 1 to 3 regional LNs, removal of ≥ 4 regional LNs), pelvic lymph node metastasis (LNM) (positive, negative and unknown); surgery (no surgery, local tumor excision, total hysterectomy), chemotherapy (no/unknown, yes) and radiotherapy (no/unknown, yes). Patients with widowed or single (never married or having a domestic partner) or divorced or separated status were all classified as unmarried22, 23. All of the eligible cases were re-identified according to the 2018 FIGO staging criteria24, 25. Median age at diagnosis was 45 years old in our study, which was used as the cutoff value for age classification. Meanwhile, the classification of tumor size and age was also based on previous researches6, 26. CCRT was defined as the addition of chemotherapy during radiotherapy. Definitive radiotherapy indicated that only radiotherapy was used in the treatment27. The endpoints of our research included overall survival (OS) and cancer-specific survival (CSS). The former was defined as the duration from diagnosis to all-cause death, and the latter referred to the duration from diagnosis to cervical AC-caused death.

Statistical analyses. Kaplan–Meier (K–M) method was employed to estimate the univariate analysis, followed by log-rank test for assessing the differences of CSS and OS among different groups. Variables with P values ≤ 0.1 in the univariate analysis were further incorporated into the multivariate Cox proportional hazard analysis. In addition, stratified analysis was performed by using Cox regression analysis. SPSS software (SPSS Inc., Chicago, USA, version 19.0) was utilized for statistical analysis, and GraphPad Prism 5 was utilized for plotting survival curves. These softwares have received permission and freely available. A two-sided P < 0.05 was considered as statistically significant. These softwares have been approved.

Results

Patients’ characteristics. A total of 3102 cervical AC patients were identified, including 2044 (65.9%) patients with stage I, 437 (14.1%) patients with stage II, 510 (16.4%) patients with stage III and 111 (3.6%) patients with stage IV. The detailed screening process was shown in Fig. 1. Patient features and therapeutic regimens were listed in Table 1. To be specific, the median age was 45 years (range 6–98 years). Among them, 11 cases (0.4%) were ≤ 18 years old, 1618 (52.20%) were ≤ 45 years old, and 422 cases (13.6%) were ≥ 65 years old. Most of cervical AC cases were of low pathological grade (grade I/II: 49.1%), had tumor size ≤ 4 cm (46.8%) and were treated by surgery (69.4%). More patients received ≥ 4 pelvic LN dissection (47.6%) and 12.6% of them had positive pelvic LN.
The median survival was 45.0 months. The 3-, 5- and 10-year CSS rates were 77.97%, 74.47% and 70.00%, respectively. Meanwhile, the 3-, 5- and 10-year OS rates were 75.56%, 71.52% and 65.17%, respectively. K–M curves stratified by FIGO stage were displayed in Fig. 2A (CSS) and Fig. 2B (OS). Notably,

| Variable                  | N (%)                |
|---------------------------|----------------------|
| Year at diagnosis         |                      |
| 2004–2007                 | 893 (28.8%)          |
| 2008–2011                 | 1062 (34.2%)         |
| 2012–2015                 | 1147 (37.0%)         |
| Insured status            |                      |
| Uninsured/unknown         | 838 (27.0%)          |
| Any medicaid/insured      | 2264 (73.0%)         |
| Insured status            |                      |
| Unmarried                 | 1512 (48.7%)         |
| Married                   | 1590 (51.3%)         |
| Age                       |                      |
| ≤ 45                      | 1618 (52.2%)         |
| > 45                      | 1484 (47.8%)         |
| Race                      |                      |
| Black                     | 237 (7.6%)           |
| White                     | 2493 (80.4%)         |
| Other                     | 372 (12.0%)          |
| Grade                     |                      |
| Grade I/II                | 1524 (49.1%)         |
| Grade III/IV              | 769 (24.8%)          |
| Unknown                   | 809 (26.1%)          |
| FIGO stage                |                      |
| Stage I                   | 2044 (65.9%)         |
| Stage II                  | 437 (14.1%)          |
| Stage III                 | 510 (16.4%)          |
| Stage IV                  | 111 (3.8%)           |
| Tumor size                |                      |
| ≤ 4 cm                    | 1453 (46.8%)         |
| > 4 cm                    | 722 (23.3%)          |
| Unknown                   | 927 (29.9%)          |
| Surgery                   |                      |
| No surgery                | 948 (30.6%)          |
| Local tumor excision      | 367 (11.8%)          |
| Total hysterectomy        | 1787 (57.6%)         |
| Lymph node dissection     |                      |
| None or biopsy            | 1553 (50.1%)         |
| 1–3                       | 72 (2.3%)            |
| ≥ 4                       | 1477 (47.6%)         |
| Pelvic lymph node metastasis |                  |
| Negative                  | 1407 (45.4%)         |
| Positive                  | 206 (6.6%)           |
| Unknown                   | 1489 (48.0%)         |
| Chemotherapy              |                      |
| No/unknown                | 1968 (63.4%)         |
| Yes                       | 1134 (36.6%)         |
| Radiotherapy              |                      |
| No/unknown                | 1845 (59.5%)         |
| Yes                       | 1257 (40.5%)         |

Table 1. The clinicopathological characteristics and treatment of the included 3102 cervical adenocarcinomas patients

**Patient survival.** The median survival was 45.0 months. The 3-, 5- and 10-year CSS rates were 77.97%, 74.47% and 70.00%, respectively. Meanwhile, the 3-, 5- and 10-year OS rates were 75.56%, 71.52% and 65.17%, respectively. K–M curves stratified by FIGO stage were displayed in Fig. 2A (CSS) and Fig. 2B (OS). Notably,
patients with stage III and IV had significantly poorer prognosis than those with stage I and II (P < 0.0001 for both). Moreover, the 5-year CSS and OS rates for patients were stage I: 90.43% and 88.08%; stage II: 55.53% and 53.19%; stage III: 23.95% and 20.45%; and stage IV: 9.77% and 8.90%. In addition, the 2-year, 5-year and 10-year survival rates of patients with different tumor grades were listed in Table 2.

Prognostic factors for survival. Univariate analysis revealed that insured status, marital status, age, race, grade, tumor size, FIGO stage, surgery, number of pelvic LN dissections, pelvic LNM, chemotherapy and radiotherapy were prognostic indicators for CSS and OS (all P < 0.05). Multivariate analysis revealed that married (HR: 0.769, 95% CI 0.662–0.894, P < 0.001) and surgery [(local tumor excision) HR: 0.568, 95% CI: 0.421–0.766, P < 0.001; (total hysterectomy) HR: 0.439, 95% CI 0.336–0.576, P < 0.001] were independent favorable prognostic factors of CSS. However, age > 45 (HR: 1.631, 95% CI 1.364–1.950, P < 0.001), grade III/IV (HR: 2.116, 95% CI 1.761–2.541, P < 0.001), tumor size > 4 cm (HR: 1.628, 95% CI 1.292–2.051, P < 0.001) and advanced FIGO stage (P < 0.001) were independent unfavorable prognostic indicators of CSS. The results of multivariate analysis in OS were similar to those of in CSS. Besides, pelvic LNM (HR: 1.648, 95% CI 1.196–2.271, P = 0.002) and chemotherapy (HR: 0.685, 95% CI 0.567–0.827, P < 0.001) were also independent prognostic factors for OS (Table 3).

Stratified analysis of the effect of chemotherapy and radiotherapy on survival. To explore the benefits of chemotherapy and radiotherapy, we performed stratified analysis of patients with different FIGO stage and surgical style. As a result, patients with stage III/IV could significantly benefit from chemotherapy (both CSS and OS) (P < 0.001), and stage II patients could benefit in terms of OS (P = 0.004). Meanwhile, patients without surgery could also significantly benefit from chemotherapy and radiotherapy (P < 0.05). In addition, only patients with stage III could significantly benefit from radiotherapy (P < 0.001) (Tables 4, 5).

Discussion
This population-based study revealed the clinicopathological features as well as survival of patients with cervical AC. Cervical AC accounts for only approximately 20–25% of all cervical carcinomas2, 3. AC is the second most common type of primary cervical cancer, secondly only to SCC28. Previous studies predominantly enrolling patients with SCC have provided most of the present therapeutic knowledge on cervical cancer29, 30. However, the different outcomes of AC have been rarely reported. Furthermore, prospective studies have not solely focused on the treatment of AC. Consequently, our understanding of the natural history, prognosis factors and optimal management of cervical AC is limited 31. To this end, we aimed at describing the clinicopathological features and treatment, as well as examining prognostic indicators for cervical AC by including a total of 3102 cervical AC patients.

Previous studies have also explored the prognostic factors of cervical AC patients. The review of 222 surgically-treated cervical AC with stage Ia2-Iia disease by Park et al. found that nodal status and parametrical

| Grade | Number | Cancer-specific survival | Overall survival |
|-------|--------|--------------------------|------------------|
|       |        | 2-year (%)  | 5-year (%)  | 10-year (%) | 2-year (%)  | 5-year (%)  | 10-year (%) |
| Grade I | 694    | 95.1        | 91.5        | 89.9        | 94.4        | 89.8        | 86.4        |
| Grade II | 830    | 89.1        | 81.8        | 76.3        | 87.7        | 79.1        | 71.9        |
| Grade III | 664    | 61.4        | 50.7        | 44.3        | 58.8        | 47.7        | 39.8        |
| Grade IV | 105    | 58.7        | 48.8        | 48.8        | 55.9        | 42.4        | 35.6        |

Table 2. The 2-year, 5-year and 10-year survival rates of patients with different tumor grades.
| Variables                      | CSS                        | OS                        | CSS                        | OS                        |
|-------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
|                               | Univariate analysis | Multivariate analysis | Univariate analysis | Multivariate analysis |
|                               | P value | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) |
| Year at diagnosis             | 0.788       | NI           | 0.591       | NI           |
| 2004–2007                     | 0.591       | 1.059 (0.863, 1.280) | 0.617       | 1.129 (0.917, 1.383) |
| 2008–2011                     | 0.617       | 1.129 (0.917, 1.383) | 0.617       | 1.129 (0.917, 1.383) |
| 2012–2015                     | 0.591       | 1.059 (0.863, 1.280) | 0.591       | 1.059 (0.863, 1.280) |
| Insured status               | 0.063       | 0.151 (0.611, 0.383) | 0.033       | 0.902       |
| Uninsured/unknown            | Reference    | Reference    | Reference    | Reference    |
| Any medicaid/insured         | 0.891 (0.761, 1.043) | 0.902 (0.780, 1.044) | Reference    | Reference    |
| Marital status               | < 0.001     | 0.001 (0.995, 0.001) | < 0.001     | 0.998       |
| Unmarried                    | Reference    | Reference    | Reference    | Reference    |
| Married                      | 0.769 (0.662, 0.894) | 0.752 (0.654, 0.865) | Reference    | Reference    |
| Age                          | < 0.001     | < 0.001 (0.001, 0.001) | < 0.001     | < 0.001     |
| ≤ 45                         | Reference    | Reference    | Reference    | Reference    |
| > 45                         | 1.631 (1.364, 1.950) | 2.027 (1.709, 2.405) | Reference    | Reference    |
| Race                         | < 0.001     | 0.383 (0.001, 0.001) | < 0.001     | 0.158       |
| Black                        | Reference    | Reference    | Reference    | Reference    |
| White                        | 0.858 (0.692, 1.065) | 0.858 | 0.824 (0.676, 1.004) | 0.055 |
| Other                        | 0.380 (0.658, 1.173) | 0.878 | 0.842 (0.644, 1.101) | 0.208 |
| Grade                        | < 0.001     | < 0.001 (0.001, 0.001) | < 0.001     | < 0.001     |
| Grade I/II                   | Reference    | Reference    | Reference    | Reference    |
| Grade III/IV                 | 2.116 (1.761, 2.541) | < 0.001 | 2.066 (1.743, 2.448) | < 0.001 |
| Unknown                      | 1.179 (0.961, 1.446) | 0.115 | 1.189 (0.987, 1.433) | 0.069 |
| FIGO stage                   | < 0.001     | < 0.001 (0.001, 0.001) | < 0.001     | < 0.001     |
| Stage I                      | Reference    | Reference    | Reference    | Reference    |
| Stage II                     | 2.679 (2.059, 3.486) | < 0.001 | 2.156 (1.698, 2.737) | < 0.001 |
| Stage III                    | 4.968 (3.843, 6.422) | < 0.001 | 4.039 (3.211, 5.080) | < 0.001 |
| Stage IV                     | 9.029 (6.645, 12.267) | < 0.001 | 6.918 (5.214, 9.178) | < 0.001 |
| Tumor size                   | < 0.001     | < 0.001 (0.001, 0.001) | < 0.001     | < 0.001     |
| ≤ 4 cm                       | Reference    | Reference    | Reference    | Reference    |
| > 4 cm                       | 1.628 (1.292, 2.051) | < 0.001 | 1.513 (1.227, 1.868) | < 0.001 |
| Unknown                      | 1.638 (1.306, 2.055) | < 0.001 | 1.546 (1.261, 1.894) | < 0.001 |
| Surgery                      | < 0.001     | < 0.001 (0.001, 0.001) | < 0.001     | < 0.001     |
| No surgery                   | Reference    | Reference    | Reference    | Reference    |
| Local tumor excision         | 0.568 (0.421, 0.766) | < 0.001 | 0.516 (0.389, 0.682) | < 0.001 |
| Total hysterectomy           | 0.439 (0.336, 0.576) | < 0.001 | 0.370 (0.287, 0.477) | < 0.001 |
| Lymph node dissection        | < 0.001     | 0.190 (0.001, 0.001) | 0.441       | Reference    |
| None or biopsy               | Reference    | Reference    | Reference    | Reference    |
| 1–3                          | 1.092 (0.586, 2.035) | 0.782 | 1.234 (0.678, 2.246) | 0.491 |
| ≥ 4                          | 0.742 (0.448, 1.229) | 0.247 | 0.922 (0.570, 1.493) | 0.743 |
| Pelvic lymph node metastasis | < 0.001     | 0.063 (0.001, 0.001) | 0.005       | Reference    |
| Negative                     | Reference    | Reference    | Reference    | Reference    |
| Positive                     | 1.481 (1.044, 2.101) | 0.028 | 1.648 (1.196, 2.271) | 0.002 |
| Unknown                      | 1.503 (0.899, 2.514) | 0.120 | 1.681 (1.030, 2.745) | 0.038 |
| Chemotherapy                 | < 0.001     | 0.067 (0.001, 0.001) | < 0.001     | < 0.001     |
| No/unknown                   | Reference    | Reference    | Reference    | Reference    |
| Yes                          | 0.823 (0.668, 1.014) | 0.685 (0.567, 0.827) | Reference    | Reference    |
| Radiotherapy                 | < 0.001     | 0.074 (0.001, 0.001) | 0.138       | Reference    |
| No/unknown                   | Reference    | Reference    | Reference    | Reference    |
| Yes                          | 0.827 (0.671, 1.019) | 0.864 (0.712, 1.048) | Reference    | Reference    |

Table 3. Univariate and multivariate analyses of cancer special survival (CSS) and overall survival (OS) for patients. CSS cancer-specific survival, OS overall survival, NI not included in the multivariate survival analysis.
involvement were independent prognostic factors for disease-free survival (DFS) and OS\textsuperscript{13}. In addition, the analysis of 46 patients with stage I-IV cervical AC revealed that FIGO stage was the only independent prognostic factor for both DFS and OS\textsuperscript{11}. A retrospective Dutch study assessing 305 cases of cervical AC found that tumor size, tumor grade and LNM remained as significant independent predictors for survival\textsuperscript{12}. Although most of these studies are small-size and single-center retrospective studies, with consistent results to ours. In addition, we also found that marital status is an independent prognostic factor for cervical AC.

The same therapeutic strategy is recommended for SCC and AC according to the present guidelines. Nevertheless, there have been no consistent data concerning the therapeutic efficacy in different histological classification\textsuperscript{7}. Surgery and radiotherapy are recommended as the primary therapeutic regimes for early-stage cervical cancer in accordance with NCCN guidelines\textsuperscript{8}. In addition, the 5-year OS rates for stage IA1 and stage IA2 lesions were 96.5% and 99.4%, respectively, for radical hysterectomy, 96.6% and 100%, respectively, for local excision, 98.4% and 96.9%, respectively, for simple hysterectomy in a study enrolling 1567 patients with cervical AC\textsuperscript{32}. Our study also found that surgery is an independent favorable prognostic factor.

Radiotherapy is an alternative option for patients who are not suitable for surgery or who refuse surgery. For patients with stage IB2-IVA cervical cancer, concurrent cisplatin based-chemoradiotherapy plus brachytherapy was the standard therapeutic regimen\textsuperscript{7}. Our study found that radiotherapy and chemotherapy could provide significant survival benefits among patients without surgery. However, in terms of tumor stage, only patients with stage III could gain significant survival benefits from radiotherapy. The worse efficacy of cervical AC is possibly caused by insensitivity of radiotherapy. Cervical AC patients have been reported to have poorer complete response (CR) as well as local control rates, therefore requiring longer time to obtain CR than SCC populations following CCRT or definitive radiotherapy\textsuperscript{29, 33, 34}. In addition to pathological type, tumor size and the type of human papilloma virus(HPV) infection were also considered to be important causes for the radiosensitivity of cervical cancer\textsuperscript{35, 36}.

In consideration of the poor outcomes of patients with cervical AC, more effective protocols are required for these patients. Adjuvant chemotherapy or neoadjuvant is a possible strategy. According to a Chinese clinical trial, 880 patients with FIGO stage IIB-IVA cervical AC were randomly assigned to receive only CCRT or CCRT with one cycle of neoadjuvant chemotherapy and two cycles of consolidation chemotherapy. Subsequently, patients treated by CCRT along with chemotherapy had better OS, DFS and local control after a median follow-up of 60 months. The above outcomes implicate that combined CCRT and chemotherapy is promising to enhance the survival of patients with cervical AC\textsuperscript{37}.

### Table 4. Stratified analysis of cancer-specific survival (CSS) and overall survival (OS) for chemotherapy in different FIGO stage and surgery style. Adjustment variables: marital status; age; grade; tumor size; pelvic lymph node metastasis; radiotherapy.

| Variables   | CSS HR (95 CI) P value | OS HR (95 CI) P value |
|-------------|------------------------|-----------------------|
| FIGO stage  |                        |                       |
| Stage I     | 1.49 (0.94, 2.37) 0.092 | 0.95 (0.65, 1.38) 0.790 |
| Stage II    | 0.68 (0.43, 1.09) 0.107 | 0.54 (0.36, 0.82) 0.004 |
| Stage III   | 0.59 (0.44, 0.79) <0.001 | 0.56 (0.43, 0.72) <0.001 |
| Stage IV    | 0.31 (0.18, 0.52) <0.001 | 0.35 (0.22, 0.55) <0.001 |
| Surgery     |                        |                       |
| No surgery  | 0.73 (0.58, 0.91) 0.006 | 0.62 (0.50, 0.76) <0.001 |
| Local tumor excision | 1.39 (0.62, 3.12) 0.430 | 0.99 (0.49, 2.01) 0.986 |
| Total hysterectomy | 4.23 (2.51, 7.11) <0.001 | 2.68 (1.69, 4.25) <0.001 |

### Table 5. Stratified analysis of cancer-specific survival (CSS) and overall survival (OS) for radiotherapy in different FIGO stage and surgery style.

| Variables   | CSS HR (95 CI) P value | OS HR (95 CI) P value |
|-------------|------------------------|-----------------------|
| FIGO stage  |                        |                       |
| Stage I     | 1.40 (0.86, 2.28) 0.179 | 1.34 (0.90, 2.01) 0.147 |
| Stage II    | 0.84 (0.50, 1.41) 0.504 | 0.88 (0.55, 1.43) 0.618 |
| Stage III   | 0.47 (0.35, 0.62) <0.001 | 0.49 (0.38, 0.65) <0.001 |
| Stage IV    | 0.74 (0.46, 1.18) 0.208 | 0.74 (0.47, 1.16) 0.191 |
| Surgery     |                        |                       |
| No surgery  | 0.57 (0.45, 0.72) <0.001 | 0.60 (0.48, 0.74) <0.001 |
| Local tumor excision | 5.76 (1.98, 16.79) 0.001 | 5.11 (2.03, 12.83) <0.001 |
| Total hysterectomy | 1.27 (0.82, 1.93) 0.287 | 1.22 (0.82, 1.82) 0.332 |
The NCI-supported SEER database is the most authoritative and largest source for tumor incidence and survival. The large-scale, publicly available SEER dataset can be reliably used to guide anti-cervical AC therapy. As far as we know, our research includes the largest subjects to investigate prognostic parameters for cervical AC in the past 10 years. Inevitably, there are still several limitations in our study. Firstly, selection bias and the effects of inaccessible variables from the SEER dataset are unavoidable due to the nonrandomized nature of our research. Secondly, information on HPV-16, comorbidities and medication use were inaccessible from SEER database, which are considered as valuable indicators for survival of cervical cancer. Thirdly, SEER fails to provide all data to completely address our hypothesis, such as detailed information on chemotherapy and radiotherapy. Nevertheless, the currently accessible information from SEER database could fit our objectives. While the above-mentioned issues should be further addressed.

Conclusions

Marital status, age, grade, tumor size, FIGO stage, pelvic LNM, surgery and chemotherapy were significantly associated with the prognosis of cervical AC. Patients without surgery could significantly benefit from chemotherapy and radiotherapy. Stage II–IV patients could significantly benefit from chemotherapy. In addition, only stage III patients could obtain significant survival benefit from radiotherapy. This is the largest study to investigate the clinicopathological characteristics and outcomes for patients with cervical AC. The present findings in our study are vital to the disease management and future prospective studies for this rare cancer.

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**Author contributions**
M.W. and Z.Z. conceived the study and searched the database and literature. M.W. and W.H. the main manuscript text. Z.Z. prepared Figs. 1 and 2 and Tables 1–4. W.H. and B.Y. revised the manuscript. All authors approved the final version.

**Competing interests**
The authors declare no competing interests.

**Additional information**

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