A Surgery-based Comprehensive Treatment Improved Prognosis in Patients with Stage IIIC Cervical Squamous Carcinoma: A Single Center Retrospective Study

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Abstract

Objective: This study intended to analyze the prognosis of patients with stage IIIC squamous cervical cancer who underwent the Obstetrics and Gynecology Hospital of Fudan University (FUOG) Treatment, and explored the factors influencing their prognosis.

Design: A retrospective study.

Setting: A large tertiary hospital specializing in obstetrics and gynecology in China.

Population or Sample: This study collected data from 717 patients with stage IIIC squamous cervical cancer who underwent FUOG Treatment in our hospital from January 2016 to December 2020.

Methods: Kaplan-Meier method was used to estimate progression-free survival (PFS) and overall survival (OS). Stratified analysis was performed to examine the risk factors.

Main Outcome Measures: The main outcomes were 3-year PFS and OS.

Results: The 3-year OS was 90.9% for patients with stage IIIC squamous cervical cancer, 91.5% for stage IIIC1 and 83.2% for stage IIIC2, respectively. The 3-year PFS was 84.8%, 85.3% for stage IIIC1 and 78.8% for stage IIIC2, respectively. Undifferentiated squamous carcinoma was an independent prognostic factor for OS (HR: 5.793, p=0.0064) and PFS (HR: 4.663, p=0.0033). Postoperative patients with standard adjuvant therapy had better 3-year OS outcomes than patients with non-standard therapy (88.4% vs 73.4%,
Patients with undifferentiated type (OR=8.471), positive parietal infiltration (OR=3.339), or tumor infiltration depth of 1/3-2/3 (OR=5.454) were more likely to have distant recurrence.

Conclusions: The prognosis of patients with stage IIIC cervical squamous carcinoma treated with the FUOG Treatment is satisfactory. However, risk factors such as undifferentiated type, positive paracervical infiltration, and non-standard adjuvant therapy can negatively affect prognosis.

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Keywords: adjuvant therapy, cervical cancer, Obsteics and Gynecology Hospital of Fudan University (FUOG) Treatment, lymph node metastasis, prognosis, recurrence, risk factors, stage IIIC

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Author Contributions
Hui WANG: Conceptualization, data curation, investigation, methodology, roles/writing - original draft; Shen LUO: Data curation, investigation, visualization, roles/writing - original draft; Ling QIU: Formal analysis, investigation, roles/writing - original draft; Hao FENG: Investigation, roles/writing - original draft; Shurong ZHU: Methodology, roles/writing - original draft; Xiaolei LIN: Data curation, methodology, software, visualization; Yanan YOU: Data curation, software; Ming LI: Visualization, software; Weili Yan: Methodology, visualization; Yuanzhou Peng: Data curation, software; Yan DU: Validation Writing - review & editing; Hua JIANG: Conceptualization, funding acquisition, project administration, resources, supervision, validation, writing - review & editing; Xin WU: Conceptualization, funding acquisition, project administration, supervision, validation, writing - review & editing.

Disclosure statement
The authors report no conflict of interest.

Introduction
Cervical cancer is one of the malignant tumors that seriously threaten women’s life and health. According to GLOBOCAN 2020, cervical cancer ranks fourth in terms of incidence and mortality rates among female malignancies worldwide. While the incidence and mortality rates of cervical cancer are decreasing in many developed countries, data from China indicate a consistent increase. Therefore, the diagnosis and treatment of cervical cancer is closely related to the health status of Chinese women.
Squamous cell carcinoma is the most common pathological type and exhibits distinct features in biological behavior, prognostic factors and radiotherapy and chemotherapy sensitivity compared to other types, which will be the focus of this study.

Lymph node metastasis is one of the most common metastasis patterns and important prognostic factors of cervical cancer. The 5-year overall survival (OS) rate of patients with cervical cancer without lymph node metastasis is 91%, but this rate decreases to 67% for patients with lymph node metastasis. According to the FIGO 2018 staging of cervical cancer, pelvic lymph node metastasis is classified as stage IIC1 and para-aortic lymph node metastasis as stage IIC2, with indications of whether the classification is based on assessment of imaging (r) or pathology (p).

According to the NCCN guidelines, the recommended treatment option for patients with stage IIC cervical cancer is concurrent radiotherapy (CCRT). According to previous studies, patients with stage IIC1 had a 5-year OS ranging from 50.3% to 73.0% and a 5-year PFS ranging from 68.9% to 70.3%, respectively. On the other hand, patients with stage IIC2 had a significantly lower 5-year OS of only 37.5% and a 5-year PFS ranging from 28.1% to 44.5%, respectively. Therefore, it is of great importance to improve the survival rate for this group.

Under the current circumstances, it has been observed that Chinese patients are more willing to accept surgical treatment options because of the unequal accessibility and varied quality of radiotherapy resources in China, the strong belief in the efficacy of complete mass resection in achieving therapeutic benefits, and the potential negative consequences of CCRT. In treating these patients, we perform a surgery-based comprehensive treatment which was generally called “the Obstetrics and Gynecology Hospital of Fudan University (FUOG) Treatment”.

In this retrospective study, we collected patients with stage IICp cervical squamous carcinoma who underwent FUOG treatment in our hospital. We analyzed the prognosis and conducted a stratified analysis to explore factors that may impact prognosis.

Method

Patients

This retrospective study included patients with squamous cervical cancer who underwent surgical treatment in the Obstetrics and Gynecology Hospital of Fudan University from January 2016 to December 2020. The inclusion criteria were as follows: 1) patients who underwent extensive total hysterectomy + pelvic lymph node dissection ± abdominal para-aortic lymph node biopsy or dissection; 2) patients whose postoperative pathology confirmed cervical squamous carcinoma; and 3) patients with stage IICp (FIGO2018). The exclusion criteria were: 1) patients with missing data; 2) patients with other malignancies during the same period; 3) patients who were enrolled in other interventional clinical trials.

Data Collection

General information, surgical and pathological data were collected through electronic medical record system of the Obstetrics and Gynecology Hospital of Fudan University. Most of the patients underwent surgery earlier than the FIGO 2018 staging system for cervical cancer released. Therefore, all patients were staged according to the FIGO 2018 staging system and postoperative pathology.

Follow-up was carried out by outpatient visits or telephone. The purpose of the study was explained to the participants before following up and was performed after obtaining informed consent. The participants were followed up yearly, and the follow-up was concluded on December 31, 2021.

The primary outcome of this study was 3-year PFS and OS. PFS was defined as the time interval from the end of treatment to disease progression, and OS was defined as the time interval from the end of treatment to the patient’s death. Disease progression was diagnosed and determined through methods including gynecological examination, tumor markers, imaging and pathological examination.
This study was approved by the Ethics Review Committee of the Obstetrics and Gynecology Hospital of Fudan University.

Treatment

All the patients were carried out by FUDAN-OG Treatment: Firstly, radical cervical cancer surgery + pelvic lymph node dissection ± abdominal paraaortic lymph node dissection/biopsy was conducted to reach R0 resection to the greatest extent. Preservation of ovary function and fertility are mainly based on the patient’s age and subjective requirements. If the tumor is ? 2 cm or the common iliac lymph node is positive for intraoperative freezing, or the preoperative evaluation of the paraaortic lymph nodes is positive, paraaortic lymph node dissection is the first choice and paraaortic lymph node biopsy is the second choice. When clearing the paraaortic lymph nodes, it is sufficient for the upper border to reach the level of the inferior mesenteric artery. If it is determined that the metastatic region of the para-aortic lymph nodes is beyond the level of the inferior mesenteric artery, the metastatic location is further cleared upward along the abdominal aorta and up to the level of the renal vessels. The common iliac lymph nodes should be sent separately for intraoperative freezing examination. Postoperative comprehensive adjuvant therapy such as CCRT and systemic chemotherapy was given based on pathological results with reference to SEDLIS criteria and the four-factor model. Postoperative comprehensive adjuvant therapy, such as CCRT and systemic chemotherapy, was administered based on pathological results, referencing the SEDLIS criteria and the four-factor model. For patients with 1+ high-risk factors or 2+ intermediate risk factors, sequential chemoradiation (SCRT) is recommended. This includes one course of systemic chemotherapy + pelvic ERBT + abdominal para-aortic extended field radiotherapy + concurrent cisplatin chemotherapy (40 mg/m2/week) + 3-6 courses of adjuvant systemic chemotherapy after radiotherapy. The preferred systemic chemotherapy regimens are paclitaxel + cisplatin/carboplatin. If the para-aortic lymph nodes or common iliac lymph node were confirmed positive, the radiotherapy field should be extended to the para-aortic lymph nodes. If the pelvic lymph nodes are positive and the para-aortic lymph nodes are negative (if a lymph node biopsy is performed without dissection, a positive result requires expanded field radiation; a negative result is equivalent to no dissection), extended field radiation is not necessary. If the pelvic lymph nodes are positive and no parietal aortic lymph node dissection is performed (lymph nodes are full with a length to diameter ratio close to 1), extended field irradiation is recommended when para-aortic lymph node metastasis is suspected by imaging.

Statistical Analysis

Numerical characteristics are described by the mean (standard deviation, SD) if normally distributed, or the median (interquartile range, IQR) if normality not met. Normality was tested by the Komogorov-Smirnov test. Univariate analyses for OS and PFS are conducted using Log rank tests and variables with p values less than 0.05 are selected into the multivariate model. Multivariate analyses for OS and PFS are conducted using Cox proportional hazards model, with statistical significance set at 0.05. Univariate and multivariate analyses for local relapse and metastasis are conducted using logistic regression models. Finally, propensity score matching is conducted to minimize confounding. All analyses are performed using R version 4.0.5.

Result

Patient Enrollment

A total of 4227 patients with squamous cervical cancer who underwent surgery was involved. According to the inclusion and exclusion criteria, a total of 717 cases included in the final analysis (Figure 1).

Patient clinicopathological characteristics

A total of 717 patients were included in this study. The general, surgical, and pathological characteristics of these patients are presented in Table 1. The average age of the patients was 49 years, with 664 patients (92.6%) classified as stage IIIC1 and 53 patients (7.4%) classified as stage IIIC2. Among the squamous cervical cancer cases, 353 (49.2%) were keratinizing, 329 (45.9%) were non-keratinizing, 11 (1.5%) were undifferentiated, and 24 (3.4%) were classified as other types.
Prognostic analysis

The median follow-up duration in this study was 33 (0-72) months. During the entire follow-up period, a total of 76 (10.60%) cases died. Among them, 64 (9.64%) deaths were recorded in stage IIIC1 and 12 (22.64%) deaths in stage IIIC2, respectively. Additionally, disease progression was observed in 112 (15.62%) cases. Specifically, 97 (14.61%) disease progression were recorded in stage IIIC1 and 15 (28.30%) in stage IIIC2, respectively. Kaplan-Meier analysis revealed that the 3-year OS for all patients with stage IIIC squamous cervical cancer was 90.9% (95%CI: 88.4%~93.4%). The 3-year OS rate was 91.5% (95%CI: 89.0%~94.0%) for stage IIIC1 patients, while 83.2% (95%CI: 72.4%~95.7%) for stage IIIC2 patients (Figure 2A). The 3-year PFS was 84.8% (95%CI: 81.9%~87.9%) for all stage IIIC squamous cervical cancer patients, 85.3% (95%CI: 82.3%~88.5%) for stage IIIC1 patients and 78.8% (95%CI: 68.0%~91.4%) for stage IIIC2 patients (Figure 2B). Patients with stage IIIC1 had a significantly better 3-year OS compared to patients with stage IIIC2 (p=0.038).

Prognostic-related factors

The Log-rank test was used to analyze clinicopathological characteristics in a univariate analysis (Table S1). The results showed that patients with pathological stage IIIC1 had a better survival prognosis compared to patients with stage IIIC2 (OS: p=0.038). Among the different pathological subtypes of squamous cervical cancer, patients with undifferentiated type had a significantly worse prognosis for survival and recurrence (OS: p=0.002, PFS: p=0.004) Patients who underwent concurrent chemoradiotherapy or concurrent chemoradiotherapy + systematic chemotherapy had a better prognosis compared to those who received radiotherapy alone, chemotherapy alone, or no adjuvant therapy (p=0.006). Patients with positive parametral infiltration had a worse prognosis for recurrence (PFS: p=0.014), with a 3-year PFS of 78.4%. Patients with a larger number of positive lymph nodes had a worse survival (OS: p=0.044), and those with a higher LNR had a worse prognosis for both survival and recurrence (OS: p=0.003; PFS: p=0.011). Metastasis to common iliac lymph nodes indicated a worse survival (OS: p=0.011), with a 3-OS of 85.8% in positive patients and 92.1% in negative patients, respectively.

Multivariate analysis was conducted to assess OS and PFS using the Cox proportional hazards model (Table 2). The results revealed that the independent prognostic factors for survival and recurrence in patients with stage IIIC cervical squamous carcinoma were the pathologic subtypes. Specifically, patients with undifferentiated pathological subtype had a 5.793-fold higher risk of death (HR: 5.793, 95% CI: 1.640-20.459, p=0.0064) and a 4.663 times higher risk of recurrence (HR: 4.663, 95% CI: 1.670-13.025, p= 0.0033) compared to those with keratinizing type.

Prognostic impact of postoperative adjuvant therapy

Patients were divided into two groups: standard and non-standard adjuvant treatment (Table S2). Among all patients, 601 (83.82%) were in the standard adjuvant therapy group, while 116 (16.18%) in the non-standard adjuvant therapy group. The standard adjuvant therapy group had younger patients (average age 48.8 vs 51.4 years, p=0.025), better physical status (ECOG score 0-1 98.33% vs 92.24%, p<0.001), a higher percentage of non-menopausal patients (59.73% vs 45.69%, p=0.005), and a lower rate of positive common iliac lymph nodes (18.14% vs 28.45%, p=0.011) compared to the non-standard adjuvant therapy group (Table S3). There were no statistically significant differences in the remaining clinicopathologic parameters between the two groups.

Propensity scores were estimated for variables that exhibited significant differences in distribution between the standard and non-standard adjuvant therapy groups. The patients in these groups were then matched at 5:1 based on their propensity scores, resulting in a total of 456 patients who met the matching criteria, with 371 patients in the standard adjuvant therapy group and 85 patients in the non-standard adjuvant therapy group. After propensity score matching, potential confounders between the two groups of patients were balanced (Table 3). Table S4 provides the complete results. After performing propensity score matching, survival analysis was conducted on the matched samples (Figure 3). The median follow-up duration was 33 months in the standard adjuvant therapy group and 34 months in the non-standard group. There was
a significant improvement in the 3-year OS in the standard group compared to the non-standard group (p=0.007). However, the difference in PFS rates between the two groups was not statistically significant (p=0.180).

Clinicopathologic features affecting patient disease progression

The recurrence of cervical cancer can be categorized into two types based on the anatomical location: local recurrence and distant metastasis. Among the 717 patients diagnosed with stage IIIC squamous cervical cancer, a total of 112 patients experienced recurrence, as indicated in Table S5. Among these recurrences, 31 patients (27.7%) had local recurrence, and 81 patients (72.3%) had distant metastases.

The clinicopathological characteristics of patients with local recurrence had no statistically significant differences compared to patients without recurrence. However, patients with distant metastasis exhibited statistically significant differences in various factors such as pathological subtype, surgical approach, parietal infiltration, postoperative adjuvant therapy, depth of stromal invasion, and common iliac lymph node status (Table S6). The results from Table 4 indicated that, after adjusting other factors, patients with undifferentiated type had a significantly higher risk of distant metastasis compared to patients with keratinized type (OR=8.471, 95% CI: 1.979 - 36.478). Additionally, patients with positive parietal infiltration had 3.339 times higher risk of distant metastasis compared to those with negative infiltration (OR=3.339, 95% CI: 1.912 - 5.860). Furthermore, patients with a tumor infiltration depth of 1/3-2/3 had 5.454 times higher risk of distant metastasis compared to patients with a depth of less than 1/3 (OR=5.454, 95% CI: 1.377 - 38.072).

Discussion
Main Findings

The results indicate that patients treated with FUOG treatment had a 3-year PFS and OS of 84.8% and 90.9%. Stage IIIC1 showed a 3-year PFS and OS of 85.3% and 91.5%, and stage IIIC2 of 78.8% and 83.2%. These results were significantly higher than the global statistics, demonstrating the FUOG treatment was advantageous over direct radiotherapy in terms of prognosis, particularly for stage IIIC2. Furthermore, for those patients, high-risk factors such as undifferentiated type, positive paracervical infiltration, and non-standard adjuvant therapy can negatively affect the prognosis of them.

Interpretation

We summarized several retrospective studies (Table S7), all of which demonstrated a poor prognosis for patients with stage IIIC cervical cancer who underwent concurrent radiotherapy. Among the 6888 patients with stage IIIC1 cervical cancer from the SEER program, those treated with surgery had a 5-year OS of 73.0%, while those who did not receive surgical treatment had a 5-year OS of 50.3%, highlighting the advantage of surgical treatment. A study conducted in Chinese patients reported a 3-year DFS of 66.3% for patients with stage IIIC1 cervical cancer who underwent chemoradiotherapy or radiotherapy, while the rate was 29.8% for patients with stage IIIC2. Compared to these previous studies, the FUOG Treatment clearly demonstrated a better prognosis.

The improved prognosis of the FUOG treatment can be attributed to four main factors. Firstly, the complete removal of the tumor mass and reduction of tumor burden, which was achieved in most surgeries, played a crucial role. The addition of CCRT + systemic chemotherapy further enhanced the effectiveness of the treatment and reduced the chances of disease recurrence. Additionally, postoperative pathology provided valuable information about the metastatic site and risk factors, enabling more targeted radiotherapy and chemotherapy treatment. Furthermore, studies have shown that the accuracy of imaging in determining lymph node metastasis is only 59-76%. It suggests the uncertainty of preoperative staging and radiotherapy regimens, and it also raises the likelihood of over- or under-treatment. These findings provided basis for the efficacy of the FUOG treatment.

Cervical squamous carcinoma can be classified based on the differential level of squamous cells into three
types: keratinizing squamous cell carcinoma (highly differentiated, large cell type), non-keratinizing squamous cell carcinoma (moderately differentiated, large cell type), and undifferentiated squamous cell carcinoma (small cell type). Our study revealed that undifferentiated squamous cervical carcinoma had a significantly higher risk of death and recurrence compared to other types, indicating a potential correlation between the differential level of carcinoma and prognosis. A cross-sectional study found that patients with undifferentiated and unknown pathologic subtypes had a 90% higher risk of death compared to those with common squamous cell carcinoma. These findings align with the results obtained in the present study.

Positive pelvic lymph nodes, parametrial infiltration, and positive vaginal margins are high-risk factors associated with the recurrence of cervical cancer. Intermediate-risk factors include LVSI (+), deep stromal invasion, and larger primary tumors. Previous studies have demonstrated that all of these risk factors are prognostically associated with lymph node-positive cervical cancers. Based on these findings, the addition of adjuvant therapy should be recommended. However, our results indicate that there were none of these risk factors were independent prognostic factors for patients with stage IIIC, except for parametrial infiltration. Parametrial infiltration also did not show a direct correlation with PFS after multivariate regression analysis. It is possible that the outcomes are influenced by our comprehensive surgical resection of the tumor mass, which effectively minimized the impact of tumor load on patients during the postoperative periods.

It is well known that once cervical cancer recurs, the survival time will be significantly reduced. Patients with distant metastases in recurrent cases generally have a worse prognosis compared to those with local recurrence. Direct metastasis of cervical cancer to systemic parenchymal organs is rare. Instead, it is more likely to spread to multiple lymphatic stations throughout the body via lymphatic vessels, leading to further metastasis to multiple sites. Therefore, the recurrence of cervical cancer often presents as distant lymph node and systemic multiple organ metastases. Our study revealed a significant increase in the risk of distant metastasis in patients with undifferentiated pathological type (p=0.0035), positive parametrial infiltration (p<0.0001), or stromal invasion depth of 1/3-2/3 (p=0.0367). The poor prognosis associated with undifferentiated carcinoma has been well-established. Notably, in patients with lymph node metastasis and parametrical infiltration, it indicates that the tumor has not only spread through the lymphatic systems but also has a propensity to spread locally. The likelihood of distant tumor metastasis is significantly higher in patients with both risk factors.

The study by William et al. showed that postoperative adjuvant concurrent chemoradiotherapy had better recurrence and prognostic outcomes compared to radiotherapy alone in cervical cancer patients with high-risk factors. Based on these findings, we recommend postoperative adjuvant therapy for patients with stage IIICp cervical cancer, specifically concurrent chemoradiotherapy with the addition of systemic chemotherapy. However, some patients may face challenges in adhering to the standard treatment plan due to economic constraints, tolerance levels for radiotherapy and chemotherapy, and limited access to medical resources for concurrent chemoradiotherapy. To further support our recommendation, we conducted this study and found that patients who received standard postoperative adjuvant therapy had significantly better 3-year OS compared to those who received non-standard therapy. Therefore, for patients with stage IIIC cervical cancer undergoing the FUOG treatment, it is crucial to adhere to postoperative adjuvant therapy to the greatest extent to ensure favorable patient prognosis.

Limitations

Our study had several limitations. Firstly, this is a single-center, single-arm retrospective study. Due to the limited availability of radiotherapy resources in our hospital, it was challenging to obtain patients in the stage IIIC radiotherapy group for squamous cervical cancer in order to directly compare their prognosis with patients who received surgery-based therapy. Additionally, there might have been some selection bias as our hospital was highly regarded in the field of obstetrics and gynecology, and usually receiving patients with high socioeconomic status and cognitive level nationwide. Secondly, due to restraint of the follow-up time, the 5-year OS and PFS data have not yet been obtained in this study. However, our study results showed satisfactory prognostic value. To provide high-quality evidence to support our findings,
a randomized controlled trial (RCT) comparing the “FUDAN-RH Treatment” with the classical regimen control is currently undergoing at our institution. According to the “FUDAN-RH Treatment”, patients were required to undergo adjuvant radiotherapy after surgical treatment, which would bring significant physical and psychological challenges. Since the retrospective study lacked evaluation of patients’ post-treatment quality of life, our research group has developed a Patient Reported Clinical Outcome Assessment Scale – CC-PRO13727. CC-PRO137 is currently being utilized to assess the quality of life of stage IIIC cervical cancer patients in 3 domains, including physiological systems, psychological related symptoms, and social life status.

Conclusion
Our study demonstrates that the FUOG treatment – a comprehensive surgery-based treatment for patients with stage IIIC squamous cervical cancer, can significantly improve prognosis. The dissemination of this program is expected to have a profound impact on the prognosis of these patients. In clinical practice, it is crucial to consider the specific type of squamous carcinoma pathology, paracellular infiltration, and the adequacy of adjuvant therapy. These factors play a significant role in determining the prognosis.

Disclosure statement
The authors report no conflict of interest.

Data availability statement
The authors confirm that the data supporting the findings of this study are available within the article.

Ethics approval
This study was approved by the Ethics Review Committee of the Obstetrics and Gynecology Hospital of Fudan University. Approval No. 2022-97; Date: Jun.24th, 2022.

Consent for publication
All patients provided written informed consent for publication of data.

Reference


**Figure Legend**

**Figure 1 Enrollment of patients with stage IIICp squamous cervical cancer**

**Figure 2 Kaplan-Meier Curve of 3-year OS (A) and PFS (B) for Patients in Stage IIIC** The curves are for all patients (red lines), patients in stage IIIC1 (green lines) and IIIC2 (blue lines), the shaded areas represent 95% confidence intervals. The 3-year overall survival were 90.9% (95%CI: 88.4%–93.4%) for all patients, 91.5% (95%CI: 89.0%–94.0%) for patients in stage IIIC1 and 83.2% (95%CI: 72.4%–95.7%) for patients in stage IIIC2, respectively (Figure 2A); the 3-year progression-free survival were 84.8% (95%CI: 81.9%–87.9%), 85.3% (95%CI: 82.3%–88.5%) and 78.8% (95%CI: 68.0%–91.4%), respectively (Figure 2B).

**Figure 3 Kaplan-Meier Curve of 3-year OS (A) and PFS (B) for the standard adjuvant therapy group and the non-standard adjuvant therapy group.** The curves are for all patients (red lines), patients in the standard adjuvant therapy group (green lines) and non-standard group (blue lines), the shaded areas represent 95% confidence intervals. The 3-year overall survival were 85.9% (95%CI: 82.3%–89.7%) for all patients, 88.4% (95%CI: 84.7%–92.2%) for patients in standard adjuvant therapy group and 73.4% (95%CI: 62.9%–85.7%) for patients in non-standard group, respectively (Figure 3A); the 3-year progression-free survival were 80.5% (95%CI: 76.4%–84.8%), 81.8% (95%CI: 77.5%–86.4%) and 73.8% (95%CI: 63.3%–86.0%), respectively (Figure 3B).

**Tables**

**Table 1 Clinical Characteristics of Patients with stage IIIC squamous cervical cancer**

**Table 2 Multivariate analysis of patients with stage IIICp cervical squamous carcinoma**
Table 3 Clinicopathologic characteristics of patients in the standard and the non-standard adjuvant therapy group before and after propensity score matching (PSM)

Table 4 Multiple logistic regression analysis of distant metastatic and non-recurrent groups

Supplementary Materials

Table S1 Univariate analysis of patients with stage IIICp cervical squamous carcinoma

Table S2 Subgroups of postoperative adjuvant therapy

Table S3 Clinicopathologic characteristics of postoperative adjuvant therapy subgroups

Table S4 Clinicopathologic information for patients in the standard adjuvant therapy group versus the non-standard group before PSM

Table S5 Subgroups of recurrence

Table S6 Clinicopathologic characteristics of patients with local recurrence, distant metastasis and non-recurrence

Table S7 Summary of retrospective studies of stage IIIC cervical cancer
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n=4227
Squamous cervical cancer patients receiving surgical treatment

n=3481 Excluded
n=2711 Negative lymph nodes
n=69 Radical Trachelectomy
n=101 Modified Radical Hysterectomy
n=577 Extraperitoneal Hysterectomy
n=23 Stage IV

n=746
Eligible stage IIIC squamous cervical cancer patients

n=29 Excluded
n=19 Missing data
n=3 Combined with other malignant tumors
n=7 Included in other interventional clinical trials

n=717
Patients included in this study

![Graphs showing overall survival and progression-free survival for different stages and subgroups of patients.](image-url)