

# Clinicopathological risk factors in the light of the revised 2018 International Federation of Gynecology and Obstetrics staging system for early cervical cancer with staging IB

## A single center retrospective study

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### Abstract

To validate the revised 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system for cervical cancer on the survival of patients who underwent radical hysterectomy for 2009 FIGO stage IB carcinomas.

We retrospectively identified and reviewed 251 patients treated with radical hysterectomy for 2009 FIGO stage IB cervical carcinomas from January 2011 to December 2016. The re-staged IB cohort consisted of 2018 FIGO stage IB1 (tumor size <2 cm), IB2 (2–3.9 cm), IB3 (≥4 cm), and IIIC1p (any pelvic nodal metastasis) cervical cancer. The univariate log-rank test and multivariate Cox regression models were performed for all potential clinic pathological risk factors based on cancer stage.

On re-staging the 251 patients with 2009 FIGO stage IB using the 2018 FIGO staging system, 96 patients (38.2%) had stage IB1, 109 patients (43.4%) had stage IB2, 28 patients (11.2%) had stage IB3, and 18 patients (7.2%) had stage IIIC1p. The 5-year overall survival (OS) rates of patients with 2018 FIGO stage IB1, IB2, IB3, and IIIC1p were 97.9%, 92.7%, 78.6%, and 61.1%, respectively. The 5-year progression-free survival rates were 97.9%, 92.7%, 63.7%, and 20.8%, respectively. Factors significantly affecting OS and disease-free survival were 2018 FIGO stage ≥IB3, histologic grade 2–3, and lymph node involvement.

The revised 2018 FIGO staging system seemed to accurately reflect the survival rate, with a distinct statistical tendency for poorer 5-year disease-free survival and OS rates with increasing stage. Women with positive lymph nodes in this classification were classified as having stage IIIC disease, which can achieve more realistic survival results than the previous staging system. The prognostic discrimination of histologic grade should be considered when revising the staging system in the future.

**Abbreviations:** CI = confidence interval, DFS = disease-free survival, FIGO = International Federation of Gynecology and Obstetrics, MRI = magnetic resonance imaging, OS = overall survival, PLN = pelvic lymph node, RR = risk ratio, SCC = squamous cell carcinoma, TP = paclitaxel and cisplatin.

**Keywords:** cervical cancer, International Federation of Gynecology and Obstetrics staging system, lymph nodes, prognosis

Editor: Deqin Ma.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

There has been no significant financial support for this work that could have influenced its outcome.

The authors have no conflicts of interest to disclose.

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How to cite this article: Zeng J, Qu P, Hu Y, Sun P, Qi J, Zhao G, Gao Y. Clinicopathological risk factors in the light of the revised 2018 International Federation of Gynecology and Obstetrics staging system for early cervical cancer with staging IB: a single center retrospective study. *Medicine* 2020;99:16 (e19714).

Received: 26 October 2019 / Received in final form: 17 February 2020 / Accepted: 1 March 2020

<http://dx.doi.org/10.1097/MD.00000000000019714>

## 1. Introduction

Unlike most solid tumors, cervical cancer is generally staged by a clinical staging system. Although the International Federation of Gynecology and Obstetrics (FIGO) cervical cancer staging guidelines allow assessment of disease severity through clinical examinations and imaging (such as chest X-ray), and even advanced imaging methods, such as positron emission tomography and computed tomography and magnetic resonance imaging (MRI), these are often used only to develop treatment strategies and clinical staging had been dominant.

The staging criteria of cervical cancer has gradually changed in the past 20 years, and in 2009, the staging criteria was revised slightly. New sub-staging was introduced for patients with early vaginal invasion. In 2018, FIGO's newly revised staging criteria<sup>[1]</sup> used imaging and pathology for staging evaluation for the first time. Lymph node metastasis (pathology or imaging) was regarded as an independent staging (stage IIIC), and the size of the tumor was used for IB1-IB3 staging. However, there was considered to be insufficient data to evaluate the prognostic value of the new staging system and effective biomarkers for identifying patients with pelvic lymph node (PLN) metastasis. The purpose of this study was to determine whether the new staging system had

more prognostic advantages. We also discuss the prospect of the potential predictive biomarkers of the clinicopathological factors to predict the prognosis of early cervical cancer after radical hysterectomy in a clinical application.

## 2. Patients and methods

We retrospectively identified and reviewed 251 patients treated in our institute for invasive cervical carcinoma between January 2011 and December 2016. We reviewed all the available medical data. The inclusion criteria were adult female (>18 years), stage IB according to the 2009 FIGO classification,<sup>[2]</sup> preoperative cervical biopsy in cases of squamous cell carcinoma (SCC), adenocarcinoma, or adenosquamous carcinoma, and treatment involving radical hysterectomy or lymphadenectomy (laparotomy or laparoscopy). The exclusion criteria were primary cone biopsy and a <6-month interval between the end of treatment and the beginning of the study.

All patients underwent radical hysterectomy and lymphadenectomy by either laparotomy or laparoscopy. Lymphadenectomy included the external iliac lymph nodes, with analysis of frozen sections. In cases with positive lymph nodes in frozen section analysis, lymphadenectomy was extended to the common iliac lymph nodes. Para-aortic lymph node dissection was performed in cases with palpably enlarged lymph nodes or enlarged lymph nodes on preoperative imaging.

Adjuvant treatment was performed in cases with positive lymph nodes and/or parametrial invasion or the presence of intra-tumoral vascular invasion; this included external pelvic radiotherapy with or without concomitant platinum-based chemotherapy.

Follow-ups were scheduled 3 months after the completion of treatment, then every 6 months for the next 5 years, and once a year from 5 years onwards. Clinical examinations, including abdominopelvic MRI or computed tomography (CT), were performed at some of the follow-ups.

We assessed safety in terms of complications. Early complications were defined as complications that occurred within 2 months of the surgical procedure, and late complications occurred more than 2 months after the surgical procedure. Complications were evaluated according to the Chassagne glossary<sup>[3]</sup>: Grade 1, mild complications that may cause some functional impairment; grade 2, moderate complications resulting in intermittent or persistent interference with normal activity; grade 3, severe complications that require surgery or invasive procedures and affect the performance status of the patient; and grade 4, any death due to complications.

Overall-survival (OS) and disease-free survival (DFS) were calculated according to the Kaplan-Meier technique. Durations of survival were calculated from the start of treatment. The endpoint was any death for OS, and local recurrence, metastasis, or any death for DFS. Survival curves were compared using the log rank test. Univariate and multivariate analyses used logistic regression with 95% confidence intervals (CIs). Measurement data were analyzed based on variance, and the comparison among groups regarding enumeration data was tested using the chi-square test. A *P*-value <.05 was considered statistically significant. Statistical analyses were performed using the SPSS 19.0 software package.

The study was approved by the Human Investigation Committee of our hospital. Written informed consent for the scientific use of the clinical data was obtained from all patients.

## 3. Results

We identified 251 patients who met the inclusion criteria. The median age of these patients was 46 (range, 24–67) years, and 4.4% of patients smoked >10 cigarettes per day. The median clinical tumor size was 2.5 cm (range, 1–8). On re-staging all patients with 2009 FIGO stage IB using the 2018 FIGO staging system, 96 patients (38.2%) had stage IB1, 109 patients (43.4%) had stage IB2, 28 patients (11.2%) had stage IB3, and 18 patients (7.2%) had stage IIIC1p. Of all the participants, 224 patients (89.2%) had SCC, 24 patients (9.6%) had adenocarcinoma, and 3 patients (1.2%) had adenosquamous carcinoma (Table 1). Initial assessments included pelvic CT in 49.9% of patients, and pelvic MRI in 50.1%. No suspicious lymph node metastasis was revealed by imaging.

According to the Querleu-Morrow classification<sup>[4]</sup> for radical surgery, 66 patients underwent laparoscopy, including 4 patients with type B, and 62 patients with type C. In total, 185 patients underwent laparotomy, including 11 patients with type B, and 174 patients with type C. The mean operative blood loss volume was 432 mL (range, 50–1100 mL): 386 mL for laparoscopy and 442 mL for laparotomy. The median total number of removed lymph nodes was 21 (0–53). After the surgical procedure, the median diameter of the tumor size was 2.3 cm (range, 1–7.5 cm). Among the total patients (251), 1.2% had parametrial invasion, 7.2% had positive PLN (14 patients with 1–3 and 4 patients with 4–6 positive PLN), and 27.1% had lymph-vascular invasion (Table 1).

Depending on the presence of high-risk factors (parametrial invasion, lymph node invasion, positive surgical margins), potentially important risk factors (Sedilis Criteria), and close surgical margins (<5 mm), only 8 patients (3.2%) received additional external beam radiation within 1 month of surgery. The type of radiotherapy was conformal radiation therapy, and the delivered dose to the pelvis was 45 Gy. In total, only 30 patients (12%) received chemotherapy, whereas 20 patients (8%) received chemoradiotherapy. Paclitaxel and carboplatin were used for treatment of adenocarcinoma or adenosquamous carcinoma. Paclitaxel and cisplatin were used for SCC (135–155 mg/m<sup>2</sup>, day 1 and 60 mg/m<sup>2</sup>, respectively) (area under the concentration time curve, 5.0–7.5, day 1). The median number of cycles of chemotherapy was 4 (1–6). In total, 76% (38/50) patients had ≥4 cycles of chemotherapy.

According to the Chassagne classification, 103 (41%) patients had grade 1 complications, 45 (17.9%) had grade 2 complications, and 3 (1.2%) had grade 3 complications. Table 2 shows the number, type, and grade of severity of intraoperative, early and late postoperative complications. In the early postoperative period, 1 patient underwent surgery for ureter and bladder injury. Early complications (<2 months from surgery) occurred in 48 (19.1%) patients; among these, 19 patients (7.6%) who underwent radical surgery with type C experienced urinary retention (duration of postoperative catheterization >14 days), 2 patients (3%) underwent laparoscopy, and 17 patients (9.2%) underwent laparotomy. In total, 13 patients (5.2%) had urinary tract infections, 2 patients (3%) underwent laparoscopy, and 11 patients (5.9%) underwent laparotomy. In total, 12 patients (4.8%) underwent gastrointestinal decompression for lower intestinal obstruction, and 4 patients (1.6%) experienced pelvic seroma that required transvaginal fine needle aspiration. With regards to long-term toxicity, there were 102 (40.6%) complications: 70 (27.9%) were grade 1, and were mostly represented

**Table 1**

**Patients' clinical and treatment characteristics and univariate analyses of risk factors of 5-year disease-free survival (DFS) and overall survival (OS).**

Variable	N (%)	DFS		OS	
		Percent	P- value	Percent	P- value
Age mean			<b>.002</b>		<b>.037</b>
≤46 yr	121 (48.2%)	81		87.6	
>46 yr	130 (51.8%)	93.1		94.6	
Menopause	105 (41.8%)		.116		.268
Smoking >10 cigarettes/d	11 (4.4%)	72.7		81.8	
None	240 (95.6%)	87.9		91.7	
Histology (%)			.363		.253
SCC	224 (89.2%)	87.9		92	
AC/ASC	27 (10.6%)	81.5		85.2	
Differentiation grade n (%)			<b>.001</b>		<b>.003</b>
High	83 (33.1%)	97.6		98.8	
Intermediate and low	168 (66.9%)	82.1		87.5	
FIGO 2018 stage			<b>&lt;.001</b>		<b>&lt;.001</b>
Ib1	96 (38.2%)	97.9		97.9	
Ib2	109 (43.4%)	92.7		92.7	
Ib3	28 (11.2%)	63.7		78.6	
IIIC1p	18 (7.2%)	20.8		61.1	
Querleu-Morrow classification			.934		.522
Type B	15 (6%)	86.7		86.7	
Type C	236 (94%)	87.3		91.5	
Operative type			.195		.218
laparoscopy	66 (26.3%)	83.3		87.9	
laparotomy	185 (73.7%)	88.6		92.4	
lymph nodes			<b>&lt;.001</b>		<b>&lt;.001</b>
Positive	18 (7.2%)	20.8		61.6	
Negative	233 (92.8%)	91.9		93.5	
Lymph-vascular invasion			<b>&lt;.001</b>		<b>.047</b>
Positive	68 (27.1%)	72.1		85.3	
Negative	183 (72.9%)	92.9		93.4	
Parametrial invasion			.175		.074
Positive	3 (1.2%)	66.7		66.7	
Negative	248 (98.8%)	87.5		91.35	
Postoperative treatment			<b>&lt;.001</b>		<b>&lt;.001</b>
Radiotherapy	8 (3.2%)	50		50	
Chemotherapy	30 (12%)	86.7		93.3	
Chemoradiotherapy	20 (8%)	30		65	
None	193 (76.9%)	94.8		95.3	

AC/ASC=adenocarcinoma or adenosquamous carcinoma, FIGO=International Federation of Gynecology and Obstetrics, SCC=squamous cell carcinoma.

by urinary complications including urgency, dysuria, and abnormal sensation; and 29 (11.6%) were grade 2, including 4 cases of moderate dyspareunia without stenosis (underwent laparoscopy), 4 (1.6%) cases of symptomatic vaginal stenosis, 4 (1.6%) cases of ureterohydronephrosis, 14 (5.6%) cases of pelvic lymphocysts, and 3 (1.2%) cases of postural incontinence. Moreover, there were 3 (1.2%) grade 3 complications, including 1 (0.4%) case of definitive colostomy and 2 (0.8%) cases of pelvic lymphocyst. No patients died as a result of post-therapeutic complications.

The median follow-up duration was 47 months (range, 6–80), and no patients were lost to follow-up. In total, 8 patients (3.2%) had only local recurrence; among these, 1 (0.4%) experienced lower vaginal recurrence, 4 (1.6%) experienced parametrial recurrence, and 1 (0.4%) experienced recurrence in the bladder. In total, 20 patients (8%) experienced metastatic relapse; among them, 7 (2.8%) experienced isolated metastatic relapse. In total,

13 patients (5.2%) experienced relapse (metastatic or/and local). The 5-year OS and DFS were 91.1% and 87.9%, respectively.

In univariate analysis, summarized in Table 1, DFS and OS were decreased in patients ≤ 46 years ( $P=.002$  and  $.037$ , respectively), with histologic grade 2–3 ( $P=.001$  and  $.003$ , respectively), FIGO 2018 stage with high level of IB (both  $P$ -values  $<.001$ ) (Fig. 1), lymph node involvement (both  $P$ -values  $<.001$ ), lymph-vascular invasion ( $P<.001$  and  $.047$ , respectively), and need for postoperative treatment (both  $P$ -values  $<.001$ ). In multivariate analysis, summarized in Table 3, that factors significantly affecting DFS and OS were as follows: 2018 FIGO stage  $\geq$  IB3 (risk ratio [RR], 6.755; 95% CI, 2.651–17.212;  $P<.001$ ; and 5.279; 95% CI, 2.269–12.283;  $P<.001$ ), histologic grade 2–3 (RR, 5.136; 95% CI, 1.215–21.708;  $P=.026$ ; and 8.136; 95% CI, 1.084–61.055;  $P=.041$ ), and lymph node involvement (RR, 2.959; 95% CI, 1.236–7.086;  $P=.015$ ; and RR, 1.632; 95% CI, 1.032–9.245;  $P=.024$ ).

The number of patients and the results of the Kaplan Meier analyses according to the previous and revised FIGO stages are shown in Tables 4 and 5. The 5-year DFS rate of the 2009 FIGO stage IB2 disease was significantly lower than that of the 2009 FIGO stage IB1 disease (52.6% vs 93.4%, respectively;  $P<.001$ ). Under the revised FIGO staging system, the 5-year DFS rates were not significantly different between stages IB2 and IB1 (92.7% vs 97.9%, respectively;  $P=.079$ ). However, the 5-year DFS rate for stage IB3 disease was significantly lower than that of stage IB2 disease (63.7% vs 92.7%, respectively;  $P=.001$ ) (Fig. 1). Similarly, stage IIIC1p disease was significantly associated with lower 5-year DFS when compared to stage IB3 disease (20.8% vs 63.7%, respectively;  $P=.006$ ) (Fig. 1).

The 5-year OS rate of the 2009 FIGO stage IB2 disease was significantly lower than that of the 2009 FIGO stage IB1 disease (67.2% vs 94.8%, respectively;  $P<.001$ ). According to the 2018 FIGO staging system, there was no significant difference in 5-year OS rates between stages IB2 and IB1 (92.7% vs 97.9%, respectively;  $P=.079$ ). However, the 5-year OS rate for stage IB3 disease was lower than that of stage IB2 disease (78.6% vs 92.7%, respectively;  $P=.049$ ) (Fig. 2). Furthermore, no significant difference was found in the 5-year OS rates between stages IB3 and IIIC1p (78.6% vs 61.1%, respectively;  $P=.23$ ) (Fig. 2). However, the 5-year OS rates appeared to drop with increasing stage (Table 5).

#### 4. Discussion

In previous FIGO criteria, only clinical and imaging findings were used for staging. The main change in the revised 2018 FIGO criteria was the addition of surgical risk factors into the staging system,<sup>[1]</sup> which mainly affected the staging of early cervical cancer. The new staging system clearly showed the significant survival differences among the 3 subgroups. Using data of 62,212 women in America,<sup>[5]</sup> 5-year survival in the FIGO 2018 schema was 91.6% (95% CI, 90.4%–92.6%) for stage IB1 tumors, 83.3% (95% CI, 81.8%–84.8%) for stage IB2 neoplasms, 76.1% (95% CI, 74.3%–77.8%) for IB3 lesions, and 60.8% (95% CI, 58.7%–62.8%) for IIIC1 lesions. In a Chinese report<sup>[6]</sup> of 362 cervical cancer patients with re-staging IB, the 5-year overall survival (OS) rates of patients with FIGO 2018 stage IB1, IB2, IB3, and IIIC1p were 95.3%, 95.1%, 90.4%, and 81.9%, compared to those of our research 97.9%, 92.7%, 78.6%, and 61.1%, respectively. Moreover, the 5-year progression-free survival rates were 94.0%, 91.0%, 88.5%, and 79.5% compared

**Table 2****Intraoperative, early, and late postoperative complications according to the Chassagne glossary.**

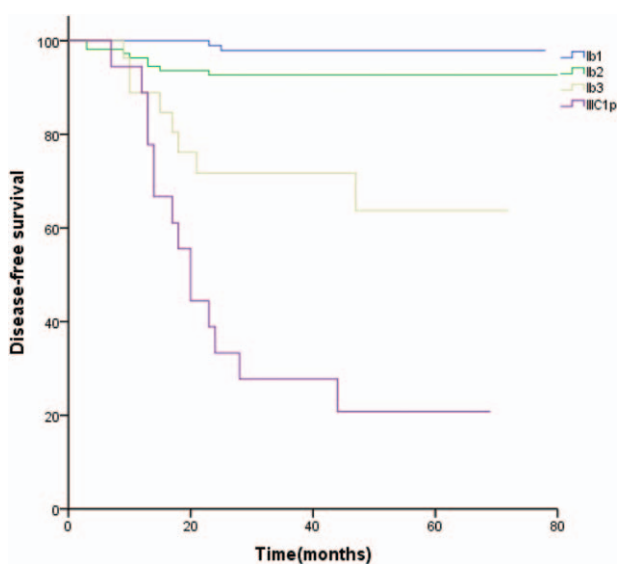
	Total (n = 251)	Laparoscopy (n = 66)	Laparotomy (n = 185)
Intraoperative complication, n (%)	1 (0.4)	1 (1.5)	0
Grade 1	<b>1 (0.4)</b>	<b>1 (1.5)</b>	<b>0</b>
Urinary			
Immediately repairable injury of ureter and bladder			
Early complications, n (%)	48 (19.1)	6 (9.1)	42 (22.7)
Grade 1	<b>32 (12.7)</b>	<b>4 (6.1)</b>	<b>28 (15.1)</b>
Urinary			
urinary retention	19 (7.6)	2 (3)	17 (9.2)
urinary tract infection	13 (5.2)	2 (3)	11 (5.9)
Grade 2	<b>16 (5.2)</b>	<b>2 (3)</b>	<b>14 (7.6)</b>
Gastrointestinal	12 (4.8)	1 (1.5)	11 (5.9)
Chronic obstruction not requiring surgery			
Pelvic soft tissues	4 (1.6)	1 (1.5)	3 (1.6)
Pelvic abscess requiring surgical drainage			
Late complications, n (%)	102 (40.6)	9 (13.6)	93 (50.3)
Grade 1	<b>70 (27.9)</b>	<b>6 (9.1)</b>	<b>64 (34.6)</b>
Urinary urgency	13 (4.8)	1 (1.5)	12 (6.5)
Stress incontinence, minor and/or occasional incontinence.	18 (7.2)	2 (3)	16 (8.6)
Dysuria	11 (4.3)	1 (1.5)	10 (5.4)
Abnormal sensation	28 (11.2)	2 (3)	26 (14.1)
Grade 2	<b>29 (11.6)</b>	<b>1 (1.5)</b>	<b>28 (15.1)</b>
Moderate dyspareunia without stenosis	4 (1.6)	0	4 (2.2)
Symptomatic vaginal stenosis	4 (1.6)	0	4 (2.2)
Ureterohydronephrosis	4 (1.6)	0	4 (2.2)
Pelvic lymphocyst	14 (5.6)	1 (1.5)	13 (7)
Postural incontinence	3 (1.2)	0	3 (1.6)
Grade 3	<b>3 (1.2)</b>	<b>1 (1.5)</b>	<b>2 (1.1)</b>
Definitive colostomy	1 (0.4)	1 (1.5)	0
Pelvic lymphocyst	2 (0.8)	0	2 (1.1)

to those of our research 97.9%, 92.7%, 63.7%, and 20.8%, respectively. In our single-institution retrospective study, the 5-year DFS and OS rates between 2018 FIGO IB1, IB2, IB3, and IIIC1p stages of disease were significantly different (both *P*-values

<.001). However, IB1 and IB2 stages had similar DFS and comparable OS, while there appeared to be a clear drop from IB2 to IB3, and from IB3 to IIIC1p. Stages  $\geq$  IB3 (IB3 and IIIC1p) significantly affected both DFS and OS (RR, 6.755; 95% CI, 2.651–17.212; *P* < .001; and 5.279; 95% CI, 2.269–12.283; *P* < .001, respectively) in multivariate analysis.

Tumor size is considered to be a prognostic factor for stage I cervical cancer, and increasing tumor size is indicative of increased lymph node involvement, higher recurrence rate, and lower survival rate.<sup>[7–9]</sup> A recent study<sup>[10]</sup> demonstrated that the survival rates were significantly different between 2018 FIGO stage IB1 and stage IB2 disease. However, we were unable to demonstrate a significant difference in 5-year OS between 2018 FIGO stage IB1 and IB2 disease. This might be due to the limited number of patients in each 2018 FIGO sub-stage in our research. However, tumor size had a discriminating outcome in terms of DFS and OS across the sub-stages of IB2 and IB3 in our study. The 5-year DFS and OS rates for stage IB3 disease were significantly lower than those of stage IB2 disease (63.7% vs 92.7%, 78.6% vs 92.7%, respectively). Similarly, stage IIIC1p disease had significantly lower DFS than stage IB3 disease (63.7% vs 20.8%, respectively), but no significant difference was found in 5-year OS rates between stages IB3 and IIIC1p.

Metastasis to local lymph nodes is the main mechanism of cervical cancer metastasis.<sup>[11]</sup> Lymph node metastasis is the main prognostic factor for the decline in the survival rate of early-stage clinical disease,<sup>[12]</sup> but it was not until 2018 that nodal status was included in the FIGO staging system.<sup>[1]</sup> Noordhuis et al<sup>[13]</sup> found



**Figure 1.** Disease-free survival curves of patients allocated to new stages according to the 2018 FIGO staging system for cervical cancer. FIGO = International Federation of Gynecology and Obstetrics.

**Table 3**

**Multivariate analyses of risk factors of 5-year disease-free survival (DFS) and overall survival (OS)<sup>a</sup>.**

Variable	DFS			OS		
	RR	95%CI	P- value	RR	95%CI	P- value
2018 FIGO stage ≥IB3	6.755	2.651–17.212	<.001	5.279	2.269–12.283	<.001
intermediate and low-grade pathology	5.136	1.215–21.708	.026	8.136	1.084–61.055	.041
Positive lymph nodes	2.959	1.236–7.086	.015	1.632	1.032–9.245	.024

RR=relative risk after adjusting for all the factors listed.

<sup>a</sup> Only variables with a P-value <.05 in univariate analysis were included in the multivariate model.

**Table 4**

**Cross table demonstrating the distribution of patients according to the 2009 FIGO and the revised 2018 FIGO staging systems.**

	2018 Stage				Total
	IB1	IB2	IB3	IIIC1p	
2009 Stage IB1	96	109	6	2	213
2009 Stage IB2	0	0	22	16	38
Total	96	109	28	18	251

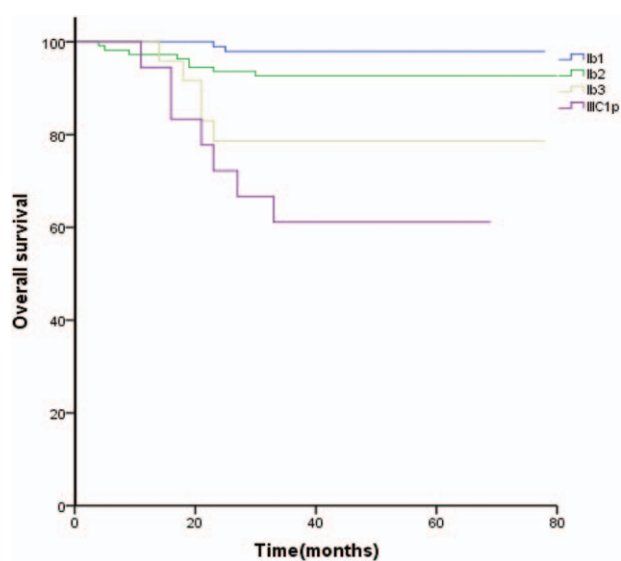
FIGO=International Federation of Gynecology and Obstetrics.

**Table 5**

**Disease-free survival and overall survival details according to the 2009 FIGO and the revised 2018 FIGO staging systems.**

Variable	N	DFS			OS		
		Number of events	Percent, %	P- value	Number of events	Percent, %	P- value
FIGO 2009 stage							
IB1	207	14	93.4		11	94.8	
IB2	44	18	52.6	<.001	11	67.2	<.001
FIGO 2018 stage							
IB1	96	2	97.9		2	97.9	
IB2	109	8	92.7	.079	8	92.7	.079
IB3	28	8	63.7	.001	5	78.6	.049
IIIC1p	18	14	20.8	.006	7	61.1	.23

FIGO=International Federation of Gynecology and Obstetrics.



**Figure 2.** Overall survival curves of patients allocated to new stages according to the 2018 FIGO staging system for cervical cancer. FIGO=International Federation of Gynecology and Obstetrics.

that patients with early-stage cervical cancer who did not have lymph node metastasis had a 5-year OS rate of 90% compared to only 65% for patients with lymph node metastasis. The survival showed a decline with an increase in stage, and this decreased significantly in patients with IIIC1p disease. Matsuo et al<sup>[10]</sup> reported the 5-year survival rate as 62.1% in 2018 FIGO stage IIIC1 disease, while the corresponding figure was 61.6% in our study. The revised 2018 FIGO staging system offered more realistic survival outcomes considering the effect of lymph node metastasis on prognosis.<sup>[11]</sup>

Histologic grade is a crucial surgical-pathologic parameter for predicting patient outcomes.<sup>[14]</sup> It is generally accepted that differentiation degree is considerably more important than the degree of infiltration with regards to determining the adjuvant treatment after radical hysterectomy<sup>[15]</sup>; this association has been extensively documented.<sup>[16]</sup> Li et al developed and accessed a surgical-pathological staging and scoring system for cervical cancer.<sup>[17]</sup> Histologic grade, as a risk factor for prognosis, has been utilized in defining surgical-pathological stages. In the current study, we also found that patients with grade 2 to 3 (intermediate/low differentiation) pathology had poor DFS and OS. Therefore, we suggested that histologic grade should be considered when revising the staging system in the future.

This was a small-sample retrospective study with a certain inherent bias. Due to the limited number of cases of each sub-stage in our research, we found no prognostic difference between sub-stages IB1 and IB2, and further prospective research is needed for the prognostic discrimination of histologic grade.

In conclusion, revised 2018 FIGO staging system is based on tumor size and lymph node involvement. It seemed to accurately reflect the survival rate with a distinct statistical tendency for poorer 5-year DFS and OS rates with increasing stage. Women with positive lymph node disease are classified as stage IIIC disease using this classification, which can achieve more realistic survival results than the previous staging system. The prognostic discrimination of histologic grade should be considered when revising the staging system in the future.

### Author contributions

**Conceptualization:** Jing Zeng, Pengpeng Qu.

**Formal analysis:** Peisong Sun.

**Methodology:** Peisong Sun.

**Project administration:** Yuanjing Hu, Pengpeng Qu.

**Supervision:** Guiling Zhao, Ji Qi, Yan Gao.

**Writing – original draft:** Jing Zeng.

**Writing – review and editing:** Jing Zeng, Pengpeng Qu.

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