




## Genitourinary Cancer

# Influence of New FIGO 2018 Staging on Treatment Outcomes in Early-Stage Cervical Cancer: A Single-Center Study

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## Abstract



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**Purpose** The aim of this article was to study survival outcomes of early-stage cervical cancer patients and impact on survival after restaging them as per International Federation of Gynecology and Obstetrics (FIGO) 2018.**Materials and Methods** A retrospective study was conducted from June 1, 2013 to May 31, 2018 in a tertiary care hospital in North India. One-hundred patients of early-stage cervical cancer (as per FIGO 2009 staging) who had been treated by surgery followed by risk based tailored adjuvant therapy in our hospital were evaluated. The clinicopathological features and survival outcomes of these patients were analyzed. These patients were then restaged as per new FIGO 2018 staging and survival outcomes between two FIGO classifications were compared.**Results** The median age of the study population was 52.5 years with median follow-up of 62.1 months. Ninety percent of our patients had more than 2 years follow-up and 59% had more than 5 years follow-up. The overall survival and relapse-free survival were 87.5 and 91.4%, respectively. The study population was then reclassified according to new FIGO 2018 staging. It was seen that the patients with stage IB1 and IB2 cervical cancer had overall survival of 91.1 and 90%, respectively. The overall survival of stage IB3 was 80% and the survival of stage IIIC1 was only 60%.**Conclusion** The new FIGO 2018 classification has a significant effect on survival outcome and in prognostication of patients with cervical cancer.

## Keywords

- ▶ early stage cervical cancer
- ▶ FIGO staging

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## Introduction

Cervical cancer has always been a clinically staged disease. Considering the advances in technology and accessibility of this technology even in low resource countries, in 2018, International Federation of Gynecology and Obstetrics (FIGO) incorporated revised staging system hoping that it would help in better prognostication and planning of the treatment. The new staging included addition of stage IB3 for tumor size more than 4 cm limited to the cervix, elimination of horizontal diameter assessment for microscopic lesion in stage IA group, and a new subdivision for stage III that is stage IIIC1 and IIIC2 with positive lymph nodes.<sup>1</sup> It was considered that these changes will impact on survival and prognosis. So, to confirm these findings, we evaluated clinicopathological features and survival outcomes of patients with early stage cervical cancer (as per FIGO 2009 staging) who had been treated by surgery followed by risk-based tailored adjuvant therapy in our center. Study population was then restaged as per new FIGO 2018 staging and survival outcomes were compared with that of FIGO 2009.

## Materials and Methods

A retrospective observational study was conducted at a tertiary care hospital in north India for patients enrolled from June 1, 2013 to May 31, 2018 over a period of 5 years. All the cases of early-stage cervical cancer (IB1 to IIA1) staged as per FIGO 2009 staging system were included. All patients underwent open radical hysterectomy with bilateral pelvic lymph node dissection. The demographic data, intraoperative details, and postoperative complications of all these patients were analyzed. The patients were stratified using postoperative histopathological features into low-risk, intermediate-risk, and high-risk categories based on Sedlis et al criteria.<sup>2</sup>

- Low risk: Pelvic lymph node negative, tumor less than 4 cm, no evidence of lymphovascular space invasion (LVSI) and less than one-third thickness of cervical stroma involvement.
- Intermediate risk: Positive LVSI, tumor size more than 4 cm, deep cervical stromal invasion.
- High risk: Pelvic lymph node involved, positive parametrial or vaginal margins.

Low-risk patients were kept on observation only. Patients with two or more intermediate risk factors were given adjuvant radiation, while patients with single high-risk factor were given adjuvant chemoradiation. Radiotherapy was given as external beam radiotherapy (EBRT) in a dose of 45 Gy over 25 fractions followed by interstitial brachytherapy as per the discretion of radiation oncologist. Chemotherapy if required was given in the form of injection cisplatin in a dose of 40 mg/m<sup>2</sup> along with EBRT.

Patients were then followed up as per standard National Comprehensive Cancer Network (NCCN) guidelines. For the first 2 years, patients were reviewed every 3 months and then 6 months for next 3 years. After 5 years, patients were

put on yearly follow-up. At every follow-up visit, all patients underwent clinical examination. Follow-up imaging for these patients was done in case of suspected recurrent or metastatic disease and symptoms.

**Statistical Analysis:** The overall survival and relapse-free survival were calculated by plotting Kaplan–Meier curves with the help of SPSS software (Version XXI). The factors influencing the survival were critically evaluated using multivariate analysis and level of significance by defining *p*-value less than 0.05 calculated using the Pearson chi-squared test.

All the histopathology reports after surgery were reclassified according to new FIGO 2018 staging and the survival outcome was then calculated and compared with previous staging using log rank test. The univariable cox regression model was used to calculate the hazard ratio.

## Results

A total of 100 patients of early-stage cervical cancer were studied from June 1, 2013 to May 31, 2018. The median age of our patients was 52.5 years. Seventy-six percent of patients had parity of three or more. The most common symptom at presentation was vaginal bleeding that was seen in 60% cases followed by vaginal discharge in 22% cases. Sixty-nine percent patients were postmenopausal, 55% patients had an exophytic growth on examination, and 84% patients had never been screened previously ([–Supplementary Table S1](#), available online only).

All clinically staged 100 patients underwent open radical hysterectomy with bilateral pelvic lymph node dissection. Ninety-one percent patients were stage IB1, 5 were IB2, and 4 were IIA1. Median duration of surgery was 150 minutes with average blood loss of 250 mL ([–Supplementary Table S2](#), available online only).

There were no intraoperative complications noted in the study population. One patient developed unilateral ureterovaginal fistula on postoperative day 10 and was managed by DJ stent for 6 weeks. The histopathology reports of all 100 patients were studied. Eighty-three patients had squamous cell carcinoma, 12 adenocarcinomas, and 5 had uncommon types including neuroendocrine, sarcoma, clear cell adenocarcinoma, adenosquamous, and villoglandular. Seventy-two patients had tumor size less than 4 cm. Lymph vascular space invasion was present in 15%, while deep stromal invasion was seen in 43%. Only eight patients had lymph node involvement on final histopathology, parametrial invasion in three patients, and positive vaginal margins in only one patient ([–Supplementary Table S3](#), available online only).

According to the final histopathology report, risk stratification was done and adjuvant treatment advised to 29 patients. Of these 29 patients, 25 patients took the advised treatment, whereas 4 patients opted for observation. The overall and relapse-free survival of all patients were calculated after a median follow-up of 62.1 months. Ninety percent of our patients had more than 2 years follow-up and 59% had more than of 5 years follow-up.

It was seen that the overall survival of 100 patients of early-stage cervical cancer was 87.5% after a median follow-

**Table 1** Reclassification to new FIGO 2018 stage

Reclassification to new FIGO 2018 stage	Frequency	Percentage
1B1 To 1B1	23	23
1B1 To 1B2	49	49
1B1 To 1B3	12	12
1B1 To IIA1	01	01
1B1 To IIA2	01	01
1B1 To IIB	01	01
1B1 To IIIC1	04	04
1B2 To 1B2	02	02
1B2 To 1B3	02	02
1B2 To IIIC1	01	01
IIA1 To 1B2	01	01
IIA1 To 1B3	01	01
IIA1 To IIA1	01	01
IIA1 To IIA2	01	01
Total	100	100

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.

up of 62.1 months. When analyzed as per FIGO 2009 stage, it was seen that in stage 1B2 (>4 cm) the overall survival fell down to 40%. This was because as per institutional policy more than 4 cm tumors were operated only if they were poor histology. Total five patients of stage 1B2 were operated, of which four were adenocarcinoma and one was papillary squamotransitional carcinoma. Three of these five patients expired. One died of chemo complications during adjuvant therapy. Two had distant relapse within first 2 years and died

of disease. This suggests that surgery may not be of benefit in large tumors with nonsquamous histology also.

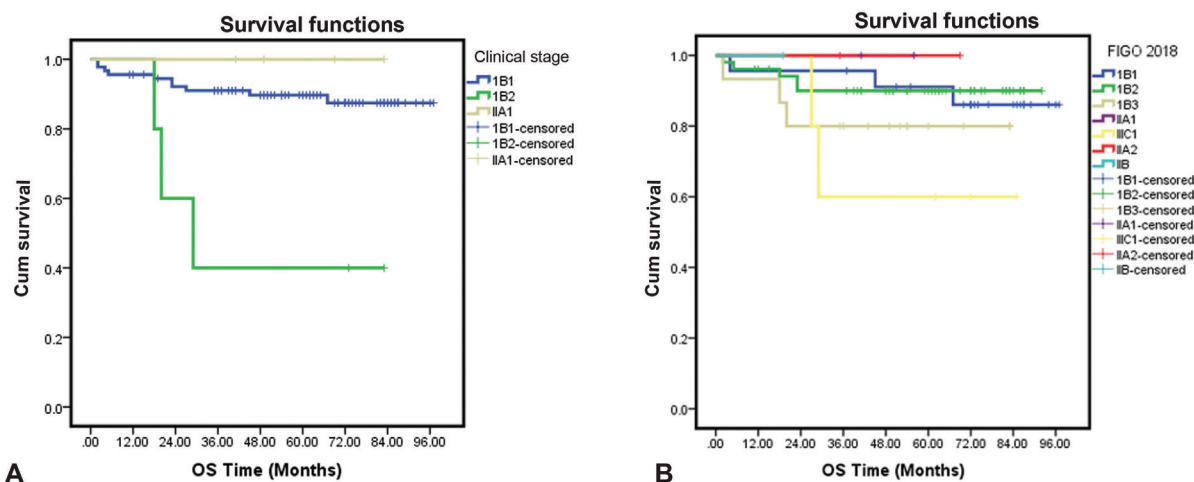
All the patients were then kept on regular follow-up. The median period of follow-up of our study population was 62.1 months. Out of the 100 patients in our study, 12% developed a relapse. The site of recurrence was vault in two cases, pelvic mass in two cases, distant metastasis in seven cases, and supraclavicular nodal metastasis in one case. Thus, locoregional recurrence was seen in four cases and eight cases had distant metastasis. All the patients who developed relapse were given adjuvant treatment, either radiation therapy or chemotherapy, and were followed up. Only one patient developed a second relapse as liver metastasis and was on palliative treatment for the same. The relapse-free survival was also calculated for the study population that was 91.4%.

Most of the patients (69%) did not develop any long-term complications. It was seen that 15% patients complained of sexual dysfunction, 9% had bladder atony, 9% had lymphedema, 3% had radiation enteritis, and 2% had radiation cystitis.

On the basis of final histopathology reports after surgery, the study population was reclassified as per FIGO 2018 classification (–Table 1). It was seen that stage change or stage migration was seen in 74% cases that was attributable to the size of the tumor and positive lymph node status.

The survival outcomes were then compared for the two groups and influence of new FIGO 2018 staging was evaluated (–Fig. 1). It was seen that the overall survival of stage 1B1 and 1B2 was 91.1 and 90%, respectively. The survival for stage 1B3 came down to 80% and for stage IIIC1, the overall survival was 60% only. The *p*-value was calculated as 0.608 that was not significant.

Presently, 82 patients are alive and healthy and in our regular follow-up, 13 patients have expired and 5 are lost to follow-up. Out of the 13 patients who expired, 5 died due to other causes and 8 died due to the disease.



**Fig. 1** (A) Stage-wise overall survival (OS) as per International Federation of Gynecology and Obstetrics (FIGO) 2009. (B) Stage-wise overall survival as per FIGO 2018.

## Discussion

In 2018, FIGO gave a new staging system for cervical carcinoma. The inclusion of lymph nodes in this staging system has led to better prognostication of patients with cervical cancer. In the present study, the patients who were reclassified as stage IB1 had survival outcome of 91.1%, stage IB2 as 90%, stage IB3 as 80%, and stage IIIC1 had survival outcome as only 60%, hence showing poor prognosis in patients with lymph node involvement. Zeng et al<sup>3</sup> conducted a retrospective study for stage IB cervical cancer patients. They analyzed 251 patients who underwent radical hysterectomy and reclassified their patients on the basis of new FIGO 2018 staging system and calculated the overall survival for all study participants. The overall survival for restaged IB1 was 97.9%; for stage IB2, it was 92.7%; for stage IB3, it was 78.6%; and for stage IIIC1, it was 61.1% that was comparable to our survival outcomes, thus, proofing the validity of the new FIGO 2018 classification and suggesting that using the new FIGO classification helps in better prognostication of the patient.

de Gregorio et al<sup>4</sup> also studied the influence of new FIGO 2018 classification on patient survival. They evaluated 265 patients of early-stage cervical cancer and restaged them on the basis of histopathology reports of radical hysterectomy specimens. The survival outcome of these patients was then calculated on the basis of new FIGO 2018 staging system. The conclusion of the study reflected a strong impact of lymph node status on the overall survival of cervical cancer patients that was also observed in our study.

Berek et al<sup>5</sup> in their study have clearly defined the multidisciplinary perspectives like role of gynecologic oncologists, pathologists, radiologists, epidemiologists in the new FIGO 2018 staging. The changes made in FIGO 2018 staging include the division of stage IB into IB1, IB2, and IB3. This is justified as each substage has not only different survival outcomes but also influences the treatment modalities. Most of the patients belonging to stage IB3 would previously require adjuvant radiotherapy post-radical hysterectomy. But, with the advent of the new 2018 FIGO staging, patients can be directly taken up for chemoradiation, thus avoiding dual modality management.

In the earlier FIGO 2009 staging, lymph node status was not included in any stage, though lymph node positivity is an important prognostic factor for cervical cancer. The addition of stage IIIC in the new FIGO 2018 staging has justified the change from clinical to clinicoradiological and pathological aspects to stage cervical cancer patients. The role of preoperative magnetic resonance imaging and guided biopsies has helped in accurate staging and appropriate adjuvant treatment for patients, thus avoiding multiple treatment toxicities.<sup>5</sup> The fall in survival with addition of stage IB3 and stage IIIC1 as compared with stage IB1 and IB2 in our study was also well depicted.

Grigsby et al<sup>6</sup> similarly compared the two FIGO staging systems (2009 versus 2019) in a cohort of 1282 patients from 1997 to 2019. In their study, 53% patients underwent stage migration as compared with 74% in our study. This difference can be due to the fact that they studied stages I to IV of cervical cancer and in our study only early-stage cervical

cancer patients who underwent primary surgery were evaluated. The attributable factors for upward stage migration in their study were also tumor size and lymph node positivity.

In India, gynecologic oncology is an upcoming subspecialization. As compared with previous literature, when surgeries were performed by a specialized professional, the outcomes of patients have seen to improve positively. In our center, all radical hysterectomies were performed by a gynecologic oncologist and adjuvant therapy tailored after discussion of all cases in the multidisciplinary tumor board meeting. Thomas et al<sup>7</sup> analyzed the treatment outcomes of early-stage cervical cancer before and after gynecologic oncology subspecialization in a tertiary care center. The introduction of subspecialization had significant impact on patient outcomes in context with decreased intraoperative and postoperative complications, with histopathology reporting of surgical specimens and also in ensuring apt and timely adjuvant therapy, thus improving overall survival. This was in comparison to our study where patients who received timely adjuvant therapy had better survival outcomes as compared with those who did not receive on being advised the same. Also, in our study population no intraoperative complications were reported and there was only 1% postoperative complication. This is attributable to the fact that our institution has a dedicated department of gynecologic oncology subspecialization.

The strengths of our study are that it is a single-center data with a dedicated gynecologic oncology unit. The decisions for treatment are finalized after multidisciplinary tumor board meetings. Appropriate case selection was done with only 29% patients being advised adjuvant therapy. The fallacies of our study are that it is a retrospective study and sample size was less and hence significant association of factors with survival could not be proven.

## Conclusion

The advent of new FIGO 2018 staging system for cervical cancer is not only validated in predicting survival outcomes and prognostication of patients but also in guiding treatment choices at all stages. Our study also showed the difference in survival with incorporation of the 2018 staging in previously staged patients who underwent primary surgery for early stage cervical cancer.

### Ethical Approval

Ethical committee approval from hospital ethics board taken.

### Funding

Nil.

### Conflict of Interest

None declared.

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