ecancermedicalscience

Comparison of Sedlis and Pretoria Gynaecologic Oncology criteria for adjuvant radiation after radical hysterectomy in non-high-risk cervical cancer

Vinotha Thomas[1a], **Monica Thiagarajan**[1b], **Dhanya Susan Thomas**[1c], **Ajit Sebastian**[1d], **Rachel Chandy**[1e], **Anitha Thomas**[1f], **Grace Rebekah**[2g], **Thomas Samuel Ram**[3h], **Abraham Peedicayil**[1i] and **Greta Dreyer**[4j]

[1]Department of Gynaecologic Oncology, Christian Medical College, Vellore, Tamil Nadu 632004, India
[2]Biostatistics, Christian Medical College, Vellore, Tamil Nadu 632004, India
[3]Department of Radiation Oncology- Unit 1, Christian Medical College, Vellore, Tamil Nadu 632004, India
[4]Gynaecologic Oncology Unit, Pretoria Academic Hospital Complex, University of Pretoria, Pretoria 0002, South Africa
[a] https://orcid.org/0000-0002-0858-2995
[b] https://orcid.org/0000-0001-7437-058X
[c] https://orcid.org/0000-0003-2230-530X
[d] https://orcid.org/0000-0002-0145-6654
[e] https://orcid.org/0000-0002-5040-8499
[f] https://orcid.org/0000-0002-5533-0184
[g] https://orcid.org/0000-0001-6279-4326
[h] https://orcid.org/0000-0001-8676-8499
[i] https://orcid.org/0000-0002-9318-566x
[j] https://orcid.org/0000-0003-0769-8408

Research

Abstract

Between 2011 and 2020, two different criteria were used in our gynaecologic oncology department to guide adjuvant radiation decisions in patients with non-high-risk cervical cancer following radical hysterectomy. This retrospective study aimed to compare oncological outcomes associated with these criteria and to assess adherence to them.

Methods: Non-high-risk patients (no lymph node, parametrial or vaginal involvement) were identified from 197 patients who underwent radical surgery between January 2011 and December 2020. Two groups were analysed: Cohort A (2011–2015), in which the Sedlis criteria were applied, and Cohort B (2016–2020), where the Pretoria Gynaecologic Oncology criteria were used. Statistical analysis included chi-square/Fisher's exact test, ANOVA and multivariate regression.

Results: Fifty patients were included in Cohort A and 105 were included in Cohort B. The adjuvant treatment rate was insignificantly higher in Cohort A (48% versus 37.1%, $p = 0.16$), with better adherence to the guideline in Cohort B (87.6% versus 82%, $p = 0.43$), although this difference was also insignificant. A substantial agreement was observed between the two criteria ($\kappa = 0.75$).

Over a median follow-up period of 60 months (0–156 months), the recurrence rates were 14% and 21% in Cohorts A and B, respectively ($p = 0.8$).

The 5-year overall survival rate was 94% in the 2011–2015 group and 90% in the 2016–2020 group ($p = 0.45$). The 5-year recurrence-free rates were 90% and 80% ($p = 0.089$).

Vaginal margins or involvement with carcinoma *in situ* (CIS) were significant recurrence predictors; vaginal involvement with CIS remained significant on multivariate analysis (OR: 3.39 and CI: 1.02–11.28).

Correspondence to: Vinotha Thomas
Email: thomasvinotha@gmail.com

ecancer 2026, **20**:2183
https://doi.org/10.3332/ecancer.2026.2183

Published: 10/08/2026
Received: 09/01/2026

Publication costs for this article were supported by *e*cancer (UK Charity number 1176307).

Conclusion: Objective, structured criteria improve treatment adherence. Vaginal CIS should be considered a high-risk factor for recurrence.

Keywords: *cervical cancer, radical hysterectomy, adjuvant radiation, carcinoma in situ*

Introduction

Early-stage cervical cancer Federation of International Obstetrics and Gynaecology (FIGO stages IA1, IA2, IB1, IB2 and select IIA1) is relatively rare in developing countries, where, in the absence of organised cervical cancer screening programmes, patients often present with bulky tumours and advanced-stage disease [1, 2]. For individuals managed with radical hysterectomy, effective postoperative risk stratification is crucial for informing adjuvant therapy to reduce their perceived risk of recurrence. Patients are typically categorised into a high-risk group with established indications for adjuvant chemoradiation and an intermediate-risk group defined by a combination of factors such as tumour size, lymphovascular space invasion (LVSI) and deep stromal invasion [3]. The landmark randomised controlled trial by Sedlis *et al* [4] showed that while adjuvant radiation therapy reduces the risk of recurrence in this intermediate-risk group, overall survival does not improve [5].

Advances in surgical and radiation techniques, as well as the integration of pathological and radiological features into the updated FIGO 2018 staging system, have intensified debates regarding the role of adjuvant radiation in patients with intermediate-risk factors. Criticism of the Sedlis trial [4] includes the poor representation of adenocarcinoma, large-sized tumours in the radiation group, the inclusion of patients based on clinical tumour size assessment, a lack of reporting regarding the extent of surgery and the use of older, conventional techniques for administering radiation [6]. Subsequent retrospective studies [7, 8] have shown no improvement in oncologic outcomes with adjuvant radiation, with data reflecting low recurrence rates of 6.3% [9] and low mortality rates of 2.5% for radical hysterectomy alone [10], highlighting the potential for favourable outcomes without adjuvant radiation.

Current guidelines recommend adjuvant radiation (National Comprehensive Cancer Network, version 25) [11] or observation [12] in this intermediate-risk group of patients who face a higher risk of local recurrence and distant metastasis compared to the low-risk group, as pooled analyses of multiple studies indicate some oncologic benefits from adjuvant radiation[13]. However, these benefits must be weighed against the associated toxicities [14].

Cervical cancer often impacts those from lower socioeconomic status and countries with low human development index (HDI) [15]. The addition of radiation to cervical cancer treatment frequently adds to morbidity and financial toxicity and worsens patient compliance with follow-up. However, in low HDI countries, cervical cancer is associated with higher recurrence rates and disease-specific mortality [16, 17]. Besides their contribution to premature death, their subsequent economic impact on bereaved families can persist for generations. Consequently, many Indian institutions continue to prescribe adjuvant radiation for intermediate-risk patients amidst ongoing debates. This retrospective study evaluates the oncologic impact of two differing criteria for adjuvant radiation in non-high-risk cervical cancer, as well as adherence to these criteria by the treating team over two specified time periods.

Patients and methods

Design

This retrospective cohort study compared two criteria for recommending adjuvant radiation after radical hysterectomy for cervical cancer. From 2011 to 2015, the criteria from Sedlis *et al* [4] were used. From 2016 onwards, risk stratification followed the criteria of the Pretoria Gynaecologic Oncology (PGO) Unit (Supplementary Figure 1). Ethical approval was granted by the institutional review board (IRB – A05-28.9.2022).

Participants

From the database of 197 patients who underwent radical hysterectomy for cervical cancer between 1 January 2011 and 31 December 2020, patients at lower risk for recurrence were identified after excluding those with high-risk factors such as lymph nodal or parametrial/vaginal margin involvement. Patients underwent types 2 or 3 radical hysterectomy (Piver classification) or radical trachelectomy based on clinical and radiological stage. Patients receiving 3–4 cycles of chemotherapy before surgery were designated as having undergone neoadjuvant chemotherapy (NACT), while those treated with radiation beforehand were categorised as neoadjuvant radiation (NART).

Patients with stage IA2–IIA1 (FIGO 2018) with non-high-risk, intermediate-risk factors for recurrence, such as the size of the tumours, depth of stromal invasion (DOSI), presence or absence of LVSI or no risk factors for recurrence, were identified and categorised into two groups as listed in the following.

1. Cohort A: Patients who underwent radical hysterectomy and pelvic lymphadenectomy between 2011 and 2015 and were assessed by the criteria proposed by Sedlis *et al* [4] to decide on adjuvant radiation.
2. Cohort B: Patients who underwent radical hysterectomy and pelvic lymphadenectomy between 2016 and 2020 and were evaluated by the criteria provided by the PGO unit to decide adjuvant radiation.

As this was a retrospective study, the institutional review board waived patient consent.

Materials

The electronic medical records of the selected patients were reviewed, and information on tumour characteristics, operative details, adjuvant treatment and oncologic outcome was obtained.

Criteria for adjuvant radiation

Based on a combination of tumour size, DOSI and LVSI, Sedlis *et al* [4] identified a group of women at an 'intermediate risk of recurrence of 30%' in the GOG 92 study who would benefit from pelvic radiation. The 'low-risk' group with no risk factor or only one intermediate-risk factor for recurrence did not benefit from radiation.

The criteria proposed by the PGO unit, in addition to the DOSI, LVSI, tumour size, combined grade of the tumour, histology (such as adenosquamous tumours), number of pelvic lymph nodes retrieved and adequacy of vaginal margins. This information was collected using a scoring sheet to ensure uniformity and reduce variability in reporting on these intermediate factors (Supplementary Figure 1). As per the PGO criteria, intermediate risk for adjuvant radiation is defined by the presence of at least two of the following factors: grade 3 or adenosquamous histology, tumour size 4–6 cm, deep one-third stromal invasion, single microscopic parametrial implant or node, vaginal margins <5 mm, <12 nodes retrieved or LVSI. This was introduced and utilised in our department from January 2016.

Adjuvant pelvic radiotherapy was delivered in most patients using three-dimensional conformal radiotherapy planned with computed tomography, to a total dose of 45–50 Gy in 25 fractions, administered five fractions per week. A few patients received radiation using the conventional four-field box technique. In accordance with institutional protocol, all patients receiving adjuvant external beam radiation also underwent vaginal brachytherapy(high dose rate) delivered using vaginal moulds at a dose of 6 Gy per fraction for 2–3 fractions. In selected patients with carcinoma *in situ* (CIS) involving the vaginal margins, in the absence of other cervical risk factors, vaginal brachytherapy alone was administered without external beam radiotherapy.

This study compared the prescription of adjuvant radiation in both periods and audited adherence to the period-specific criteria for adjuvant radiation. The oncologic outcome following treatment of non-high-risk cervical cancer in the 2011–2015 period was compared with the 2016–2020 period.

All patients were hypothetically assessed under both criteria, and agreement was analysed using Cohen's Kappa statistic.

Definitions

Adjuvant radiation received included external beam radiation to the pelvis and/or brachytherapy post-surgery. Chemoradiation included concurrent cisplatin. Patients receiving radiation – with or without chemotherapy – contrary to period-specific guidelines, were classified as overtreated, while those who did not receive guideline-recommended radiation were classified as undertreated. Adherence to guidelines was calculated after excluding individuals who were either undertreated or overtreated.

During surveillance, recurrence confined to the vagina/pelvis was considered as 'local recurrence'. Metastasis outside the true pelvis was labelled as distant recurrence. Patients diagnosed with vaginal intraepithelial neoplasia grade 3 (VaIN 3) during follow-up were also classified as having local recurrence, because these patients carry a high risk of subsequent invasive pelvic recurrence after a prior diagnosis of cervical cancer, unlike patients with a history of preinvasive disease alone.

The recurrence-free period was calculated from the surgery date to the earliest of the recurrence detection or the last follow-up.

Disease-specific survival was calculated from the date of surgery to the date of death due to disease or the last follow-up.

Overall survival was calculated from the date of surgery to the date of death due to any cause or the last follow-up.

Statistical analysis

The data were analysed using SPSS v26 (IBM, Armonk, NY, USA). Continuous variables were summarised using means, standard deviations, medians and ranges, whereas counts and percentages were used for categorical variables. Chi-square/Fisher test, ANOVA and multivariate regression were used to assess risk factors for recurrence. The log-rank test and Kaplan–Meier curves were used to assess differences in patient survival between the two time periods.

Results

There were 155 patients with non-high-risk factors who were included in the study, following surgery, comprising 50 in Cohort A (2011–2015) and 105 in Cohort B (2016–2020).

Patient characteristics

Both cohorts were similar in age, surgical treatment and tumour characteristics. Three patients received NACT before referral to our centre. One patient with idiopathic thrombocytopenia was referred for surgery after 18 fractions of radiation due to persistent thrombocytopenia. Cohort B demonstrated better histological categorisation of adenocarcinoma compared to Cohort A. Following surgery, two patients in Cohort A and 11 in Cohort B had vaginal margins involved by CIS (Table 1).

Adjuvant treatment and adherence to treatment guidelines

Both groups exhibited similar intermediate-risk factors, including deep stromal invasion (>50%), LVSI and tumour size greater than 2 cm (Table 2). Among 105 patients, 55 (35.5%) had no risk factors for recurrence. Of the 13 patients with CIS at the vaginal margin, four without additional risks were advised observation after surgery.

Despite the PGO criteria incorporating four additional factors, the adjuvant radiation rate was lower in Cohort B (37.1% versus 48.0%), although not statistically significant. One patient received only brachytherapy due to CIS at the vaginal margins. Four patients in Cohort B received chemotherapy along with radiation for clear cell histology and high-grade histology, which was considered overtreatment. Adherence to PGO criteria was higher (87.6% versus 82.0%), but the difference was not statistically significant. A total of nine patients did not follow the prescribed radiation (default rates: Cohort A versus B: 4% versus 6.7%). All patients who initiated radiation completed the treatment, although two experienced treatment delay due to pyelonephritis during radiation, one of whom required percutaneous nephrostomy and ureteric stenting.

Table 1. Patient characteristics.

Patient characteristics	Cohort A 2011–2015 (*N* = 50)	Cohort B 2016–2020 (*N* = 105)	Statistical significance (*p*-value)
Mean age (years, standard deviation, SD*)	49.24 (10.29)	47.98 (11.35)	0.507
Primary treatment*			
Type 2 radical hysterectomy	10 (20%)	10 (9.5%)	
Type 3 radical hysterectomy	40 (80%)	88 (83.8%)	
Laparoscopic radical hysterectomy	-	1 (1%)	0.29
NACT, type 3 radical hysterectomy		3 (2.9%)	
NART, type 3 radical hysterectomy		1 (1%)	
Trachelectomy		2 (1.09%)	
FIGO stage			
Stage IA1 and I A2	4 (28.6%)	15 (14.3%)	
Stage I B1	20 (18%)	32 (30.5%)	
Stage I B2	18 (36%)	47 (44.8%)	0.169
Stage I B3	8 (16%)	6 (5.7%)	
Stage II A1	-	2 (1.9%)	
Stage II A2 (post NACT)	-	1 (1.0%)	
Stage II B (post NART)	-	2 (1.9%)	
Tumour characteristics			
Median size of tumour (cm, IQR)	2.5 (1.2, 3.8)	2.45 (1.2, 3.5)	0.794
Histology (no. of patients, %)			0.542
Squamous carcinoma	39 (78%)	83 (79%)	
Adenocarcinoma	11 (22%)	22 (21%)	
Adenosquamous	-	2	
Clear cell		3	
Villoglandular adenocarcinoma		1	
Mesonephric carcinoma		1	
Differentiation of tumour (no. of patients, %)			0.597
Grade 1	12 (24%)	32 (30.4%)	
Grade 2	28 (56%)	50 (47.61%)	
Grade 3	10 (20%)	23 (21.9%)	
Stromal invasion:			0.814
Superficial 1/3rd	20 (40%)	45 (42.85%)	
Middle 1/3rd	12 (24%)	20 (19.04%)	
Deep 1/3rd	18 (36%)	40 (38.09 %)	
Presence of LVSI	8 (16%)	24 (22.9%)	0.271
Vaginal margin involved by intraepithelial neoplasia	2 (4%)	11 (10.5%)	0.17

SD, standard deviation. Cm, centimeter. IQR, interquartile. NACT, neoadjuvant chemotherapy. NART, neoadjuvant radiation. FIGO, International Federation of Gynecology and Obstetrics

* All radical hysterectomies and trachelectomies were combined with pelvic lymph nodal dissection

Radiation treatment rates were higher among patients with large tumours (>IB3), grade 3 histology, deep stromal invasion and LVSI (Table 3). Cohort B showed a significant increase in radiation use for grade 3 histology (15.2% versus 33.3%, $p = 0.03$), but the proportions were similar to those in Cohort A.

Cohen's Kappa correlation coefficient showed substantial agreement between Sedlis and PGO criteria (Table 4). Eighteen of the 102 patients (17.6%) who would have been advised observation by the Sedlis criteria, however, would have been advised radiation by the PGO criteria (Tables 2–4).

Table 2. Comparison of recurrence risk factors, treatment details and guideline adherence between Cohorts A (2011–2015) and B (2016–2020).

Characteristic	Cohort A 2011–2015 (*N* = 50)	Cohort B 2016–2020 (*N* = 105)	Statistical significance (*p*-value)
Presence of risk factors for recurrence			
No risk factors	19 (38%)	36 (34.3%)	0.87
1 intermediate-risk factor	15 (30%)	34 (32.4%)	
2 intermediate-risk factors	13 (26%)	31 (29.5%)	
3 intermediate-risk factors	3 (6%)	4 (3.8%)	
Treatment details			
Observation	26 (52%)	66 (62.9%)	0.206
Adjuvant radiation	24 (48%)	39 (37.1%)	
Radiation	21 (42%)	27 (25.7%)	
Chemoradiation	1 (2%)	4 (3.9%)	
Vaginal brachytherapy	0	1 (1%)	
Defaulted	2 (4%)	7 (6.7%)	
Adherence to treatment guideline as per time	41/50 (82%)	92/105 (87.6%)	**0.432**
Overtreatment	8	9	
Undertreatment	1	4	

Table 3. Risk factor comparison by adjuvant radiation therapy status in two patient cohorts.

Risk factor	Overall cohort 2011–2020			Group A 2011–2015 (*n* = 50)			Group B 2016–2020 (*n* = 105)			Test of proportions Group A versus group B
	Surgery only (*n* = 92, %)	Adjuvant treatment (*n* = 63, %)	*p*-value	Surgery only (*n* = 26, %)	Adjuvant treatment (*n* = 24, %)	*p*-value	Surgery only (*n* = 66, %)	Adjuvant treatment (*n* = 39, %)	*p*-value	
FIGO stage ≥IB3	4 (4.3)	15 (23.8)	0.00	0	8 (33.3)	0.00	4 (6.1)	7 (17.9)	0.055	0.478
Nonsquamous histology	21 (22.8)	12 (19.0)	0.57	6 (23.1)	5 (20.8)	0.84	15 (22.7)	7 (17.9)	0.561	0.861
Grade 3	14 (15.2)	19 (30.2)	0.029	4 (15.4)	6 (25.0)	0.39	10 (15.2)	13 (33.3)	0.03	0.725
Stroma invasion > 50%	27 (17.4)	53 (34.2)	0.00	8 (16.0)	20 (40)	0.00	19 (18.1)	33 (31.4)	0.00	0.846
Presence of LVSI	7 (7.6)	25 (39.7)	0.00	1 (3.81)	7 (29.2)	0.018	6 (9.1)	18 (75.0)	0.00	0.438
CIS at vaginal margin	5 (5.4)	8 (12.7)	0.10	1 (3.8)	1 (3.8)	0.93	4 (6.1)	7 (17.9)	0.05	Insufficient

FIGO, International Federation of Gynecology and Obstetrics. LVSI, lymphovascular space invasion. CIS, carcinoma *in situ*

Table 4. Correlation between PGO criteria and Sedlis criteria.

	Sedlis			
PGO criteria		Radiation	Observation	Cohen's Kappa
	Radiation	50	18	0.754 ($p < 0.001$)
	Observation	0	84	

Follow-up and recurrence

After a median follow-up of 90.5 months for Cohort A and 49 months for Cohort B, there were 29 recurrences (18.7%), primarily within the first 5 years (26 cases), and were commonly confined to the pelvis (16/29) (Table 5). Cohorts A and B had 7 (14%) and 22 (21%) recurrences, respectively, with no statistically significant difference between them (Table 5).

Among the local recurrences, 8/17 presented with VaIN 3, detected by abnormal vaginal cytology, which was then confirmed by colposcopy-guided vaginal biopsy. One patient was diagnosed when the vaginal biopsy showed VaIN 3, 20 months after initial surgery, who then opted for vaginal brachytherapy as there was no other evidence of disease.

Five patients diagnosed with VaIN3 underwent vaginectomy, of whom four patients developed macroscopic pelvic recurrence during follow-up, and the 5th patient developed vulval cancer subsequently. Two patients refused further treatment, one of whom developed pelvic recurrence. After excluding two patients who had received NACT, the median duration from surgery to development of VaIN 3 was 15 months (range of 7–54 months) in six patients.

The eight other patients with local recurrences received chemoradiation, while one patient refused treatment.

Distant recurrence was most common in the lungs (6/12, 50%), with other sites including the peritoneum (1), liver (1), nodes (2), brain (1) and bone (1).

Nine patients treated after recurrence became disease-free, while 14 died from the disease, with three additional deaths due to other causes.

The overall recurrence-free rate was 81.2%, with 90% in Cohort A and 80% in Cohort B at 5 years ($p = 0.089$). The overall survival rate was 89%. Over a median follow-up period of 92 months (0–156) in Cohort A and 55 months (0–100) in Cohort B, 88% and 89.5% were alive in each cohort. Five-year survival rates were 94% (47/50) and 90% (95/155) ($p = 0.459$).

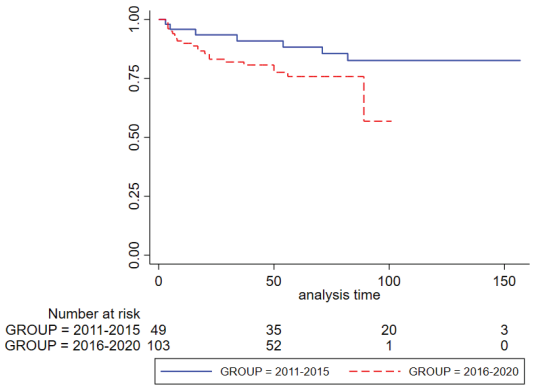
Kaplan–Meier curves showed comparable recurrence-free rates for both cohorts (log-rank test, $p = 0.105$, Figure 1), and similar survival rates (log-rank test, $p = 0.753$, Figure 2). After excluding patients who received NACT/NART, those who defaulted adjuvant radiation and patients whose adjuvant treatment decisions did not adhere to the guideline, Kaplan–Meier curves showed no difference in recurrence-free periods in both cohorts (Figure 1b). Kaplan–Meier curves also showed that adjuvant radiation status did not alter the recurrence-free period (Figure 3).

Risk factors for recurrence

Risk factors for recurrence such as FIGO stage higher than I B2, nonsquamous histology, grade of tumour, presence of LVSI, stromal invasion more than 50% and outer 3rd stromal invasion, involvement of the uterus by tumour, lymph node counts lower than 12, presence of 2 or more intermediate-risk factors, vaginal margin involvement by CIS or any vaginal involvement or close margins and nonprescription of adjuvant radiation were explored using univariate categorical analysis (Table 6). Vaginal cuff margin involvement by CIS and any vaginal involvement by CIS (excluding vaginal cuff margin involvement) or close vaginal margins (less than 5 mm) were found to be significant risk factors for recurrence. On univariate Cox regression analysis, patients with CIS in the vaginal cuff margin and CIS of vagina/close margin (excluding margin involvement) had a hazard ratio (HR) of 4.43 and 4.20, respectively, for recurrence (Table 7). Any vaginal involvement/close margin remained a significant risk factor for recurrence in multivariate regression analysis (HR: 3.39, 1.02–11.28). The use of Sedlis criteria in Cohort A or PGO criteria in Cohort B, or the use of radiation, made no difference in the risk of recurrence (Tables 6 and 7).

Table 5. Follow-up.

Clinical parameter	Cohort A 2011–2015 (*N* = 50)	Cohort B 2016–2020 (*N* = 105)	Statistical significance *p*-value
Median duration of follow-up	90.50 months (0–157)	49 months (0–101)	
Recurrence status			
No follow-up	3 (6%)	2 (1.9%)	
No recurrence	40 (80%)	81 (77.1%)	
Recurrence	7 (14%)	22 (21.0%)	0.804
Local	4 (8%)	13 (12.4%)	
Local and distant		1 (1%)	
Distant	3 (6%)	8 (7.6%)	
Status after diagnosis of recurrence			
Disease free after treatment of recurrence	2 (4%)	7 (6.7%)	
Under treatment for recurrence	-	3 (2.9%)	0.442
Alive with disease	1 (2%)	2 (1.9%)	
Died due to recurrence	4 (8%)	10 (9.5%)	



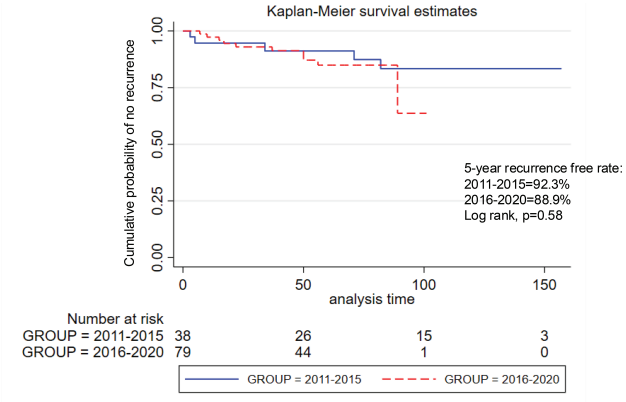


Figure 1. (a): Kaplan-Meier curves of recurrence-free survival after surgery for non-high-risk cervical cancer in 2011–2015 group and and 2016-2020 group. (b): Kaplan-Meier curves showing recurrence-free survival after surgery for non-high-risk cervical cancer in the 2011–2015 and 2016–2020 groups, excluding those who received NACT, NART, or were non-adherent and non-compliant.

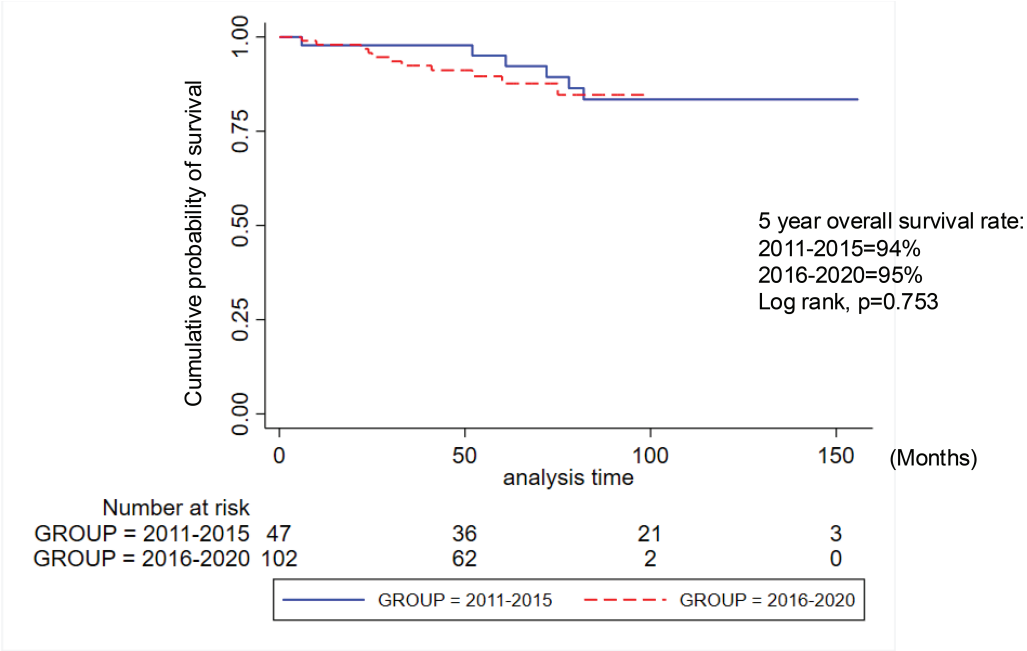


Figure 2. Kaplan Meier curves of overall survival for non high risk cervical cancer in 2011–2015 group and 2016–2020 group.

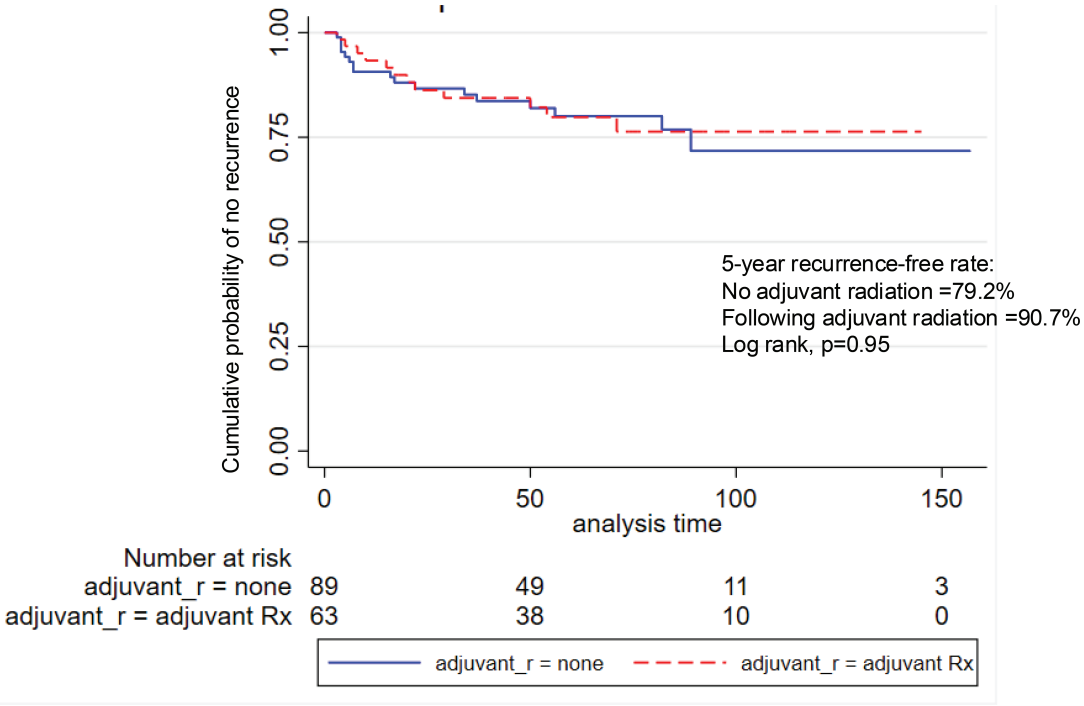


Figure 3. Kaplan-Meier curves of recurrence-free survival based on presence or absence of adjuvant radiation following surgery for non high risk cervical cancer.

Table 6. Univariate categorical analysis of risk factors associated with recurrence.

Risk factors for recurrence (no. of patients = 155)	Recurrence (*n* = 29)	*p*-value
Stage ≥ 1B3 (19, 12.3%)	5 (17.2%)	0.35*
Nonsquamous histology (31, 20.7%)	6 (20.7%)	0.499*
Poorly differentiated (33, 22%)	10 (34.5%)	0.08
LVSI (32, 20.6%)	6 (20.7%)	1*
>50% stromal invasion (80, 51.6%)	17 (58.6%)	0.207
Outer 3rd stromal invasion (58, 37.4%)	14(48.3%)	0.441
Uterine involvement (22, 14.1%)	4 (13.8%)	1*
Lymph node yield <12 (51, 32.9%)	10 (33.9%)	0.951
≥2 intermediate-risk factors (51, 32.9%)	13 (44.8%)	0.108
CIS in vaginal margin (13, 8.3%)	**6 (20.7%)**	**0.017***
Vaginal involvement and close margins (27, 17.4%)	**11 (37.9%)**	**0.001**
No adjuvant radiation (92, 59.35%)	17 (79.3%)	0.92

*Fischer's exact test
LVSI, lymph vascular space invasion
CIS, carcinoma *in situ*

Table 7. Univariate and multivariate cox regression analysis of recurrence risk factors.

Risk factor	Univariate analysis			Multivariate analysis		
	HR	95%CI	*p*-value	HR	95%CI	*p*-value
Cohort A versus Cohort B	1.628	0.644–4.114	0.303	-		
≥Stage I B3	0.600	0.197–1.825	0.368			
Nonsquamous histology	1.045	0.387–2.827	0.93			
Uterus involvement	0.960	0.299–3.085	0.945			
LN<12	0.95	0.46–2.224	0.906			
LVSI	1.003	0.370–2.71	0.995			
CIS at vaginal margins	4.43	1.36–14.40	0.013	1.54	0.33–11.28	0.582
Any vaginal involvement/close margin (excluding margin)	4.20	1.68–10.49	0.002	3.39	1.02–11.28	0.046
Adjuvant radiation	1.038	0.457–2.357	0.929			

HR, Hazard ratio; CI, Confidence interval; LN, lymph node; LVSI, lymphovascular space invasion; CIS, carcinoma *in situ*

Discussion

Summary of results

This study compared two criteria for adjuvant radiation across two patient cohorts: the Sedlis criteria (2011–2015) and the PGO criteria (2016–2020), which included additional factors such as adenosquamous histology and lymph node count. High-risk patients were excluded, and those with no or intermediate risk were included. The findings indicated a nonstatistical reduction in adjuvant radiation rates and

improved guideline adherence with the PGO criteria, with both cohorts showing similar recurrence and survival rates. Notably, CIS in the vaginal cuff margin and close margin were significant recurrence risk factors, and adjuvant radiation did not prevent recurrence.

Continuing the debate: to observe, improve or modify the approach

Radical hysterectomy with pelvic lymphadenectomy and adequate surgical margins provides the best oncologic survival advantage for early cervical cancer. Adjuvant radiation may benefit patients at increased risk of recurrence, particularly those with intermediate-risk factors, who face a recurrence risk of approximately 15% [18]. The site of recurrence significantly impacts survival, with loco-regional recurrences having a 70.5% salvage rate compared with 36.8% for lung metastases [19]. Sedlis *et al* [4] demonstrated that adjuvant radiation can lower local and distant recurrence rates, with a 30% reduction in mortality; however, this difference was not statistically significant.

In this heterogeneous group of early-stage patients, where risk is predicted based on a combination of risk factors, various alternative prognostic factors have been studied over the past three decades to identify select patients within the intermediate-risk group who would benefit from radiation therapy. These additional risk factors include histological features such as adenocarcinoma or adenosquamous histology [20], tumour budding [21] and tumour-free distance [22]. Developments in understanding tumour biology have assigned a high recurrence rate to human papillomavirus-independent carcinoma, but these have not been factored into adjuvant treatment modification [23].

Although the prognostic implications of these factors require further validation, individual risk stratification for patients in this heterogeneous group using nomograms can help personalise the assessment of recurrence risk [20]. The definition of the intermediate-risk group has evolved over the past three decades with the advancement of surgical techniques, such as sentinel node mapping and ultra-staging, which allow the identification of micrometastases and further refine its definition. Evidence from prospective randomised controlled trials for treatment de-escalation, comparing observation versus adjuvant radiation following radical hysterectomy, is awaited [24]. On the contrary, the benefit of adding chemotherapy to radiation has been explored and shown to be debatable [25, 26]. The results of GOG 0263, which studied the addition of chemotherapy to adjuvant radiation in patients with intermediate-risk factors and LVSI, did not benefit recurrence-free or overall survival but did transiently worsen quality of life [27].

In a previously published study from our institution that included high-, intermediate- and low-risk patients, the recurrence rates ranged from 16% to 26% with high utilisation of adjuvant radiation [28, 29]. In 2016, the PGO criteria instead of the Sedlis criteria were adopted in our institution to triage the non-high-risk group for adjuvant radiation and reduce recurrence rates by including additional prognostic factors while ensuring adherence to protocol by using a scoring sheet by ticking risk factors, the combination of which would assign a risk score. The utilisation of the PGO criteria on a scoring sheet showed a nonstatistically significant difference in adjuvant radiation rates (11%) and a 5% improvement in adherence to guidelines. However, 17.6% of cases, as advised by the Sedlis criteria, would have been recommended for radiation by the PGO criteria. As there was no reduction in recurrence rates in either cohort, the use of additional risk factors to triage for adjuvant radiation cannot be recommended. Following a nomogram or scoring sheet to assign risk, rather than relying on mental assignment and perception of increased risk, can help avoid undertreatment and overtreatment of this group, which has a relatively lower risk of recurrence.

Risk of recurrence in the low-intermediate-risk group

Our retrospective study recruited non-high-risk patients after excluding patients with high-risk histology such as gastric carcinoma, neuroendocrine carcinoma and patients with involved pelvic lymph nodes, parametrium or vaginal margins (with cancer). We included patients with no documented risk factors and those with intermediate risk factors and reapplied both the Sedlis and PGO criteria to assess adherence and oncologic outcome. We included patients who had received NACT in another institution and one patient who did not tolerate upfront radiation. Although these patients would have made the cohort heterogeneous, they were included because their surgical specimens showed no high-risk factors, and they were not advised to undergo adjuvant therapy after surgery. However, these patients were not included in the survival analysis in Figure 1b, which showed no difference in the cumulative probability of recurrence in the homogenised cohort.

The overall recurrence rate was 18%, and most recurrences were in the pelvis (17/29, 58.6%), with a high fatality rate following distant recurrences (10/12, 83%), similar to reports from other published cohorts [30]. Nearly 80% of the recurrences occurred in the group that did not receive radiation; however, this difference was not statistically significant.

Involvement of the vagina or vaginal margins with CIS at the time of radical surgery was associated with a statistically significant risk of recurrence, understandably so, as their vagina was already involved, and vaginal CIS can be a multifocal disease. Despite the wide confidence intervals, this finding is hypothesis-generating and has not been reported so far, to the best of our knowledge. While brachytherapy can be offered to patients with CIS in the vaginal margins to ensure local control [31], most patients with CIS of the vagina but not of the margins are usually followed up.

Our study also reports that the patients who were already treated for cervical cancer and who, on follow-up, develop VaIN have an increased risk of progression to invasive, recurrent cancer. Despite small numbers, four of the five patients who underwent vaginectomy soon developed pelvic recurrence. In post-treatment surveillance of cervical cancer, VaIN 3 should therefore preferably be treated with either brachytherapy or full-thickness excision of the vagina to avoid recurrence at the vaginal vault [32]. Treatment of VaIN with loop electrosurgical excision can be hazardous as it is difficult to control the depth of excision [33]. Vaginectomy or mere removal of the vaginal skin can be reserved for patients who were previously treated with PGO of the cervix [34]. In this study, we suggest that vaginal CIS during surveillance following radical hysterectomy often precedes invasive recurrent cervical cancer.

The strengths of this study include the following.

1. The study reflects real-world challenges faced in a tertiary teaching centre in a low- and middle-income country, where cervical cancer is prevalent, patients often present with advanced disease and recurrence rates are high.
2. The study highlights that additional factors in treatment criteria (beyond existing ones) did not significantly reduce recurrence rates in non-high-risk patients following radical hysterectomy.
3. While not statistically significant, using a scoring sheet format ensured easier identification of risk factors and better compliance with treatment guidelines.
4. The study identifies vaginal CIS, even without margin involvement, as a significant risk factor for pelvic recurrence.

The study's weaknesses are as follows.

1. Including patients with varying levels of recurrence risk, including those at negligible risk who still received radiation, complicates the interpretation of treatment efficacy and recurrence outcomes. However, these patients were included because the low-intermediate risk group is heterogeneous in the real world.
2. Being a teaching institution, the radicality of surgeries could not be standardised. This variability may have influenced the outcomes, introducing a potential confounder into the analysis.
3. As a retrospective study, it is prone to selection bias and incomplete data. This design also limits the ability to establish causal relationships. This retrospective study also spans a decade across two different time zones, during which considerable changes have occurred in patient selection for surgery, in the understanding and reporting of cervical cancer pathology, treatment approaches and radiation delivery techniques. With a greater understanding of the role of advanced radiological imaging, the use of magnetic resonance imaging increased in Cohort B.
4. The relatively small cohort sizes, particularly for Cohort A, reduce the statistical power of comparisons and may have prevented some findings from achieving statistical significance. Similarly, due to small numbers, CIS of the vaginal margin and any vaginal involvement with CIS/close margins have been reported to be risk factors for recurrence with wide confidence intervals.

Conclusion

This study highlights the real-world challenges in managing cervical cancer in a low- and middle-income country, emphasising the high burden of disease and recurrence despite advancements in treatment protocols. While including additional factors in treatment guidelines did

not significantly reduce recurrence rates in non-high-risk patients, structured postoperative risk stratification tools may improve adherence to adjuvant treatment recommendations without significantly altering oncologic outcomes. Vaginal CIS and close margins were identified as significant risk factors for pelvic recurrence; however, given the small sample size, event rates and retrospective design, larger prospective studies are needed to validate this before incorporation into risk stratification guidelines.

Conflicts of interest

The authors have no conflicts of interest to declare.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Author contributions

VT and MT conceived the study design. VT, MT, DST, AJ, RC, AT, TR and AP were involved in data collection, interpretation and conclusion. GR was involved in data analysis and interpretation. GD was involved in data interpretation and had introduced the PGO criteria to the institution. VT prepared the manuscript, which was reviewed and approved by all the co-authors. All authors have agreed to be responsible for the published research.

Data availability

The data will be made available on reasonable request.

References

1. Lavigne AW, Triedman SA, and Randall TC, *et al* (2017) **Cervical cancer in low and middle-income countries: addressing barriers to radiotherapy delivery** *Gynecol Oncol Rep* **22** 16–20 https://doi.org/10.1016/j.gore.2017.08.004 PMID: 28948205 PMCID: 5602511
2. Mahantshetty U, Lavanya G, and Grover S, *et al* (2021) **Incidence, treatment and outcomes of cervical cancer in low- and middle-income countries** *Clin Oncol (R Coll Radiol)* **33**(9) e363–e371 https://doi.org/10.1016/j.clon.2021.07.001 PMID: 34274204
3. Delgado G, Bundy B, and Zaino R, *et al* (1990) **Prospective surgical-pathological study of disease-free interval in patients with stage IB squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study** *Gynecol Oncol* **38**(3) 352–357 https://doi.org/10.1016/0090-8258(90)90072-S PMID: 2227547
4. Sedlis A, Bundy BN, and Rotman MZ, *et al* (1999) **A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: a Gynecologic Oncology Group Study** *Gynecol Oncol* **73**(2) 177–183 https://doi.org/10.1006/gyno.1999.5387 PMID: 10329031
5. Rotman M, Sedlis A, and Piedmonte MR, *et al* (2006) **A phase III randomized trial of postoperative pelvic irradiation in Stage IB cervical carcinoma with poor prognostic features: follow-up of a gynecologic oncology group study** *Int J Radiat Oncol Biol Phys* **65**(1) 169–176 https://doi.org/10.1016/j.ijrobp.2005.10.019 PMID: 16427212
6. Rodriguez J, Viveros-Carreño D, and Pareja R (2022) **Adjuvant treatment after radical surgery for cervical cancer with intermediate risk factors: is it time for an update?** *Int J Gynecol Cancer* **32**(10) 1219–1226 https://doi.org/10.1136/ijgc-2022-003735 PMID: 36511890

7. Matsuo K, Shimada M, and Matsuzaki S, *et al* (2024) **Assessment of postoperative therapy de-escalation for early-stage, intermediate-risk cervical cancer** *Int J Gynecol Cancer* **34**(9) 1349–1358 https://doi.org/10.1136/ijgc-2024-005597 PMID: 39107048

8. Nasioudis D, Latif NA, and Giuntoli Ii RL, *et al* (2021) **Role of adjuvant radiation therapy after radical hysterectomy in patients with stage IB cervical carcinoma and intermediate risk factors** *Int J Gynecol Cancer* **31**(6) 829–834 https://doi.org/10.1136/ijgc-2021-002489 PMID: 33962994

9. Cibula D, Abu-Rustum NR, and Fischerova D, *et al* (2018) **Surgical treatment of "intermediate risk" lymph node negative cervical cancer patients without adjuvant radiotherapy-a retrospective cohort study and review of the literature** *Gynecol Oncol* **151**(3) 438–443 https://doi.org/10.1016/j.ygyno.2018.10.018 PMID: 30348519 PMCID: 6615487

10. Tuscharoenporn T, Muangmool T, and Charoenkwan K (2023) **Adjuvant pelvic radiation versus observation in intermediate-risk early-stage cervical cancer patients following primary radical surgery: a propensity score-adjusted analysis** *J Gynecol Oncol* **34**(4) 42 https://doi.org/10.3802/jgo.2023.34.e42

11. NCCN guidelines version 1.2025 cervical cancer [https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf] Date accessed: 27/01/25

12. Cibula D, Raspollini MR, and Planchamp F, *et al* (2023) **ESGO/ESTRO/ESP Guidelines for the management of patients with cervical cancer - update 2023** *Int J Gynecol Cancer* **33**(5) 649–666 https://doi.org/10.1136/ijgc-2023-004429 PMID: 37127326 PMCID: 10176411

13. Sagi-Dain L, Abol-Fol S, and Lavie O, *et al* (2019) **Cervical cancer with intermediate risk factors: is there a role for adjuvant radiotherapy? A systematic review and a meta-analysis** *Gynecol Obstet Invest* **84**(6) 606–615 https://doi.org/10.1159/000501683 PMID: 31344705

14. Chopra S, Gupta S, and Kannan S, *et al* (2021) **Late toxicity after adjuvant conventional radiation versus image-guided intensity-modulated radiotherapy for cervical cancer (PARCER): a randomized controlled trial** *J Clin Oncol* **39**(33) 3682–3692 https://doi.org/10.1200/JCO.20.02530

15. Huang J, Deng Y, and Boakye D, *et al* (2022) **Global distribution, risk factors, and recent trends for cervical cancer: a worldwide country-level analysis** *Gynecol Oncol* **164**(1) 85–92 https://doi.org/10.1016/j.ygyno.2021.11.005

16. Fu C, Wang C, and Qian Q, *et al* (2023) **A novel predictor for the use of concurrent chemotherapy in early-stage cervical cancer with intermediate-risk factors** *Gynecol Oncol Rep* **48** 101228 [https://doi.org/10.1016/j.gore.2023.101228] PMID: 37389134 PMCID: 10300080

17. Momenimovahed Z, Mazidimoradi A, and Maroofi P, *et al* (2023) **Global, regional and national burden, incidence, and mortality of cervical cancer** *Cancer Rep (Hoboken)* **6**(3) 1756 [https://doi.org/10.1002/cnr2.1756]

18. Van Der Velden J, Mom CH, and Van Lonkhuijzen L, *et al* (2019) **Analysis of isolated loco-regional recurrence rate in intermediate risk early cervical cancer after a type C2 radical hysterectomy without adjuvant radiotherapy** *Int J Gynecol Cancer* **29**(5) 874–878 https://doi.org/10.1136/ijgc-2019-000445 PMID: 31133601

19. Chen Y, Zhu Y, and Wu J (2021) **Prognosis of early stage cervical cancer according to patterns of recurrence** *Cancer Manag Res* **13** 8131–8136 https://doi.org/10.2147/CMAR.S314384 PMID: 34737641 PMCID: 8560325

20. Levinson K, Beavis AL, and Purdy C, *et al* (2021) **Beyond Sedlis-a novel histology-specific nomogram for predicting cervical cancer recurrence risk: an NRG/GOG ancillary analysis** *Gynecol Oncol* **162**(3) 532–538 https://doi.org/10.1016/j.ygyno.2021.06.017 PMID: 34217544 PMCID: 8405564

21. Park JY, Chong GO, and Park JY, *et al* (2020) **Tumour budding in cervical cancer as a prognostic factor and its possible role as an additional intermediate-risk factor** *Gynecol Oncol* **159**(1) 157–163 https://doi.org/10.1016/j.ygyno.2020.07.030 PMID: 32741542

22. Saatli B, Olgan S, and Gorken IB, *et al* (2014) **Tumour-free distance from outermost layer of cervix is of prognostic value in surgically treated cervical cancer patients: a multicenter study** *Arch Gynecol Obstet* **289**(6) 1331–1335 https://doi.org/10.1007/s00404-014-3142-7 PMID: 24435497

23. Li D, Huang S, and Liu K, *et al* (2022) **Clinicopathological characteristics and survival outcomes in human papillomavirus independent cervical cancer: a propensity score matched analysis** *Int J Gynecol Cancer* **32**(5) 599–605 https://doi.org/10.1136/ijgc-2021-003159

24. Cibula D, Borčinová M, and Kocian R, *et al* (2022) **CERVANTES: an international randomized trial of radical surgery followed by adjuvant (chemo) radiation versus no further treatment in patients with early-stage, intermediate-risk cervical cancer (CEEGOG-CX-05; ENGOT-CX16)** *Int J Gynecol Cancer* **32**(10) 1327–1331 https://doi.org/10.1136/ijgc-2022-003918 PMID: 36100282

25. Guo Q, Wang R, and Jin D, *et al* (2022) **Comparison of adjuvant chemoradiotherapy versus radiotherapy in early-stage cervical cancer patients with intermediate-risk factors: a systematic review and meta-analysis** *Taiwan J Obstet Gynecol* **61**(1) 15–23 https://doi.org/10.1016/j.tjog.2021.11.006 PMID: 35181028

26. Agustí N, Viveros-Carreño D, and Wu CF, *et al* (2025) **Adjuvant chemoradiotherapy vs radiotherapy alone for patients with intermediate-risk cervical cancer** *JAMA Oncol* **11**(5) 511–518 https://doi.org/10.1001/jamaoncol.2025.0146 PMID: 40079948 PMCID: 11907360

27. Ryu SY, Deng W, and Albuquerque K, *et al* (2025) **Randomized phase III trial of adjuvant radiation versus chemoradiation in intermediate-risk, early-stage cervical cancer following radical hysterectomy and lymphadenectomy: results from NRG Oncology/GOG-263/KGOG 1008** *Ann Oncol* **25**(25) 4700 [https://doi.org/10.1016/j.annonc.2025.09.003]

28. Gnanamalar A, Peedicayil A, and Sebastian A, *et al* (2019) **The surgical and oncological outcomes of radical hysterectomy for early cervical cancer** *Indian J Gynecologic Oncol* **17** 16 https://doi.org/10.1007/s40944-019-0259-4

29. Thomas V, Chandy RG, and Sebastian A, *et al* (2021) **Treatment outcomes of early carcinoma cervix before and after sub-specialization** *Indian J Surg Oncol* **12**(1) 78–85 https://doi.org/10.1007/s13193-020-01228-x PMID: 33814836 PMCID: 7960842

30. Ramirez PT, Robledo KP, and Frumovitz M, *et al* (2024) **LACC trial: final analysis on overall survival comparing open versus minimally invasive radical hysterectomy for early-stage cervical cancer** *J Clin Oncol* **42**(23) 2741–2746 https://doi.org/10.1200/JCO.23.02335 PMID: 38810208

31. Chopra S, Ranjan N, and Mittal P (2022) **Postoperative adjuvant radiation for cervical cancer: reflections on the evidence and a peek into the future** *Int J Gynecol Cancer* **32**(3) 225–230 https://doi.org/10.1136/ijgc-2021-002528 PMID: 35256407

32. Abe A, Matoda M, and Okamoto S, *et al* (2015) **Resection of the vaginal vault for vaginal recurrence of cervical cancer after hysterectomy and brachytherapy** *World J Surgical Oncol* **13** 137 https://doi.org/10.1186/s12957-015-0495-8

33. Powell JL and Asbery DS (2000) **Treatment of vaginal dysplasia: just a simple loop electrosurgical excision procedure?** *Am J Obstet Gynecol* **182**(3) 731–732 https://doi.org/10.1067/mob.2000.102701 PMID: 10739540

34. Kesic V, Carcopino X, and Preti M, *et al* (2023) **The European Society of Gynaecological Oncology (ESGO), the International Society for the Study of Vulvovaginal Disease (ISSVD), the European College for the Study of Vulval Disease (ECSVD), and the European Federation for Colposcopy (EFC) consensus statement on the management of vaginal intraepithelial neoplasia** *Int J Gynecol Cancer* **33**(4) 446–461 https://doi.org/10.1136/ijgc-2022-004213 PMID: 36958755 PMCID: 10086489

Supplementary information

ADJUVANT TREATMENT for CA CX

STICKER/NAME	DATE of SURGERY	
	DATE of MDT	
	CO-MORBIDITIES	
	TICK APPROPRIATE BLOCK FOR EACH PARAMETER, NOTE FINAL DECISION	

CERVICAL CANCER:		GUIDELINES FOR ADJUVANT TREATMENT after Radical hysterectomy & pelvic lymphadenectomy (> 12 NODES)		
FIGO STAGE I and IIA		DISEASE CONFINED TO THE UTERINE CERVIX (AND UPPER VAGINA)		
PARAMETER	**LOW RISK**	**INTERMED RISK**	**HIGH RISK**	**NOTES**
HISTOLOGY TYPE	Squamous / Adeno Ca	Adeno-squamous / Gr 3		Neuro-endocrine: Consider CT
TUMOUR SIZE	< 2cm = small / 2 cm + = medium	4 cm to 6 cm = large	➢ 6 cm	6 cm + : ChemoRadiotherapy
DEPTH OF INVASION	Inner 2/3 stroma = not deep	Outer 1/3 stroma = deep		Full thickness: Radiotherapy at least
PARAMETRIUM	Negative/not reported	Single microscopic implant OR parametrial node	Any involvement more than microscopic or nodal	
SURGICAL MARGINS	5mm + = radical	<5mm = close	< 2mm = involved	Count margin behind bladder reflection as worst of surgical margin OR depth of invasion, NOT both
NODES	Negative and at least 12 nodes reported	< 12nodes reported Single microscopic	>1 Microscopic 1+ Macroscopic Extra-capsular spread	Single microscopic:pelvic chemoRT Para-aortic +: CRT and consider extended field
LYMPHOVASCULAR INV	Negative / not reported	LVS involved		
THERAPY RECOMMENDATION	**No adjuvant therapy**	**2 + Factors: Radiotherapy**	**1 + Factor: Chemo-radiation**	**MDT DECISION:**

Supplementary Figure 1. Criteria from the PGO unit.