Original Article

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Incidence of Adjuvant Radiation Therapy after Radical Hysterectomy and Preoperative Prognostic Factors in Cervical Cancer Patients (Stage IA2-IIA1) in Lampang Hospital, Ten Years' Experience

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Abstract:

Introduction: For early-stage cervical cancer (IA2–IIA1), radical hysterectomy with pelvic lymphadenectomy and primary chemoradiation offer comparable cure rates. However, some patients require adjuvant radiation therapy after surgery. Combined modality therapy can lead to significant long-term complications.

Objectives: The objective of this study is to evaluate the incidence of adjuvant radiation therapy after radical hysterectomy and to identify preoperative prognostic factors in early-stage cervical cancer (stages IA2–IIA1) at Lampang Hospital.

Materials and Method: This retrospective cohort study included early-stage cervical cancer patients who underwent radical hysterectomy with pelvic lymphadenectomy (2014–2023). Preoperative risk factors for adjuvant radiotherapy, including tumor size, diagnostic method, tumor type, vaginal bleeding, and suspected vaginal invasion, were analyzed using univariate and multivariate logistic regression in Stata 18.0.

Results: Out of 173 patients, 69 (39.9%) received postoperative adjuvant radiotherapy. Preoperative vaginal bleeding (aOR 2.48, 95% CI: 1.21-5.06; p = 0.013) and suspected vaginal invasion (aOR 10.92, 95% CI: 1.23-97.09; p = 0.032) were significantly associated with the need for adjuvant radiation therapy after radical hysterectomy. Tumor size > 4 cm was associated with an increased risk in the univariable analysis (OR 2.76, p = 0.016). Other factors, including non-SCCA histology and gross lesions, showed trends toward increased risk but did not reach statistical significance.

Conclusion: At Lampang Hospital, 39.9% of patients received postoperative radiation therapy after radical hysterectomy. Preoperative clinical examinations alone are insufficient to predict radiation therapy needs. Advanced imaging techniques, such as CT or MRI,

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are used to aid in treatment planning. In resource-limited settings, evaluations should focus on high-risk patients with vaginal bleeding, suspected vaginal invasion, or tumors > 4 cm.

Keywords: Uterine Cervical Neoplasms, Radical Hysterectomy, Radiotherapy, Adjuvant

Introduction

For early-stage cervical cancer (stages IA2 to IIA1), the primary treatment options are radical hysterectomy with pelvic lymphadenectomy or primary chemoradiation therapy, both of which have comparable cure rates.[1,2] However, after surgery, some patients may require adjuvant radiation therapy to reduce the risk of recurrence,[3] but this can increase the risk of complications from combined modality therapy.[4]

Postoperative adjuvant radiation therapy is used to improve overall and progression-free survival in high-risk patients, such as involvement of lymph nodes, residual tumors, and parametrium invasion.[5] Additionally, it's also given to patients with two or more intermediate-risk factors, like deep stromal invasion, large tumor size, or lymphovascular space invasion (LVSI), based on the 'Sedlis criteria.[3]

Late complications of radical hysterectomy include voiding dysfunction, lymphocyst, and lymphedema.[6] Pelvic radiation therapy, can lead to long-term complications such as vaginal stenosis, dyspareunia, rectal bleeding or stenosis, radiation cystitis, fistulas, and lymphedema.[7] Therefore, receiving combined modality therapy can lead to increased complications from both treatment methods, particularly urethral strictures, radiation cystitis, and vulvovaginal fistulas, which significantly reduce quality of life and may result in further complications.[4,8]

After the FIGO (International Federation of Gynecology and Obstetrics) staging system was revised in 2018[9], imaging, along with clinical examination, became essential for accurately determining the stage of the patient's cancer. The available resources can determine the stage of the patient's cancer using pelvic ultrasound, MRI, CT, or PET/CT scans. These imaging methods give the details about tumor size, parametrial involvement, and lymph node status.[10] In our setting, although CT and MRI are available, prolonged wait times—often exceeding four weeks—limit their routine use. As a result, early-stage cervical cancer is often evaluated based on clinical staging alone. Understanding preoperative prognostic factors for adjuvant radiation therapy is essential for selecting the most appropriate treatment for each patient.

The objective of this study is to evaluate the incidence of adjuvant radiation therapy after radical hysterectomy and to identify preoperative prognostic factors in early-stage cervical cancer (stages IA2–IIA1) at Lampang Hospital, where preoperative access to CT or MRI is limited.

Materials and Method

This retrospective observational cohort study reviewed medical records from the Department of Obstetrics and Gynecology, Lampang Hospital, with approval from the Research Ethics Committee (REC No. 032/66). The inclusion criteria were patients with FIGO stage IA2-IIA1 cervical cancer (classified according to FIGO 2018 but staged without CT/MRI)) who underwent radical hysterectomy with pelvic lymphadenectomy between January 1, 2014, and December 31, 2023.

The primary outcome was the proportion of patients who required adjuvant radiation therapy following

radical hysterectomy. The secondary outcome was the identification of preoperative clinical factors associated with the need for adjuvant radiation therapy, including tumor size, histology, vaginal bleeding, and suspected vaginal invasion. These preoperative risks were based on prognostic factors described in the FIGO 2018 staging system and prior studies on risk stratification (Sedlis criteria and Peters criteria). These included the diagnostic method (Loop Electrosurgical Excision Procedure (LEEP) or gross biopsy), tumor size, cancer type (squamous cell carcinoma (SCCA) or non-SCCA), suspected vaginal extension, lymphovascular invasion, and FIGO stage. CT and MRI findings were excluded from this analysis. Postoperative prognostic factors were identified based on the Peters criteria[5] (at least one of: positive lymph node metastasis, parametrial invasion, or positive surgical margins) and the Sedlis criteria[3] (at least two of: lymphovascular space invasion (LVSI), deep stromal invasion (≥1/3 stromal thickness), or a tumor diameter ≥ 4 cm). General demographic and clinical data collected included age, menopausal status, and presenting symptoms.

The exclusion criteria included patients who received incomplete treatment, those who refused treatment, those with incomplete medical record information, and those who received neoadjuvant chemotherapy.

Patients were divided into two groups. Patients who underwent surgery without additional treatment were classified as the "Surgery alone" group, while those who received adjuvant radiotherapy (including both radiation therapy alone and concurrent chemo-radiation therapy) were classified as the "Surgery and RT" group.

The analysis was performed using Stata software, version 18.0. Descriptive statistics were used to assess the prevalence of adjuvant radiation therapy. Demographic data were presented as percentages, means, standard deviations, medians, and interquartile ranges. Independent t-tests or Mann-Whitney U tests were used to compare continuous variables between groups, and Fisher's exact tests were applied for categorical variables. Statistical significance was set at $p < 0.05$. Univariable and multivariable logistic regression analyses evaluated preoperative prognostic factors for adjuvant radiation therapy, presenting odds ratios (OR), adjusted odds ratios (aORs), and 95% confidence intervals (95% CIs).

Results

In the past 10 years, a total of 202 patients underwent radical hysterectomy with pelvic lymphadenectomy. Out of these, we excluded 29 patients: 18 had other types of cancer, 4 had noncancerous conditions, and 7 had no available information. As a result, 173 patients diagnosed with cervical cancer at stages IA2 to IIA1 underwent surgery. Following surgery, 69 patients (39.9%) received adjuvant radiation therapy.

Table 1 summarizes the baseline characteristics of the study population. The mean age was 48.5 years (range: 24–72 years). Menopause was present in 42.2% of patients, and 39.3% had a history of LEEP. Most patients were classified as FIGO stages IB1–IB3 (85.6%). Histopathological findings showed squamous cell carcinoma (SCCA) in 62.4%, and 84.4% of tumors measured less than 4 cm in diameter. The median tumor size was significantly larger in the Surgery and RT group (2.0 cm vs 1.3 cm, $p = 0.001$), with preoperative tumor size also being significantly greater in this group ($p = 0.007$). Additionally, vaginal bleeding ($p = 0.002$) and suspected vaginal invasion ($p = 0.005$) were more frequent in the Surgery and RT group. However, there were no significant differences between groups in mean age, BMI, menopausal status,

parity, or histopathology. The recurrence rate was 5.77% for the Surgery group and 15.9% for the Surgery plus RT group (p = 0.052). However, this difference was not statistically significant.

Table 1 Baseline characteristics (N=173)

Baseline characteristics	**Total n (%) 173**	**Surgery alone n (%) 104 (60.12)**	**Surgery and RT n (%) 69 (39.88)**	**P-value**
Age (Mean ± SD)	48.5 ± 9.5	47.7 ± 8.7	49.8 ± 10.5	0.137
BMI (Mean ± SD)	23.6 ± 3.5	23.7 ± 3.1	23.5 ± 4.0	0.620
Menopause status				0.365
No	100 (57.8)	63 (60.6)	37 (53.6)	
Yes	73 (42.2)	41(39.4)	32 (46.4)	
Parity				0.459
0	16 (9.2)	11 (10.6)	5 (7.2)	
≥ 1	157 (90.8)	93 (89.4)	64 (92.8)	
Presenting symptoms*				
None	79 (45.7)	57 (71.0)	22 (29.0)	**0.007**
Vaginal bleeding	85 (49.1)	41 (39.4)	44 (63.8)	**0.002**
Abnormal pain	24 (13.9)	17 (16.4)	7 (10.1)	0.248
Diagnostic method				0.052
LEEP or cone biopsy	68 (39.3)	47 (45.2)	21 (30.4)	
Gross lesion	105 (60.7)	57 (54.8)	48 (69.6)	
Tumor size (Pre-op, cm)				**0.007**
≤ 2 cm	94 (54.3)	66 (63.5)	28 (40.6)	
2 – 4 cm.	52 (30.1)	27 (25.9)	25 (36.2)	
> 4 cm.	27 (15.6)	11(10.6)	16 (23.2)	
Median [IQR]	1.5 [0.9-3.0]	1.2 [0.7-3.0]	2.0 [1.2-3.5]	**0.001**
Vaginal Invasion (Suspected)	8 (4.6)	1 (1.0)	7 (10.1)	**0.005**
Pathology				0.506
SCCA	108 (62.4)	67 (64.4)	41 (59.4)	
Non-SCCA	65 (37.6)	37 (35.6)	28 (40.6)	
LVSI positive (Pre-op) (Missing data = 61)**				
	29 (16.8)	15 (14.4)	14 (20.3)	0.596

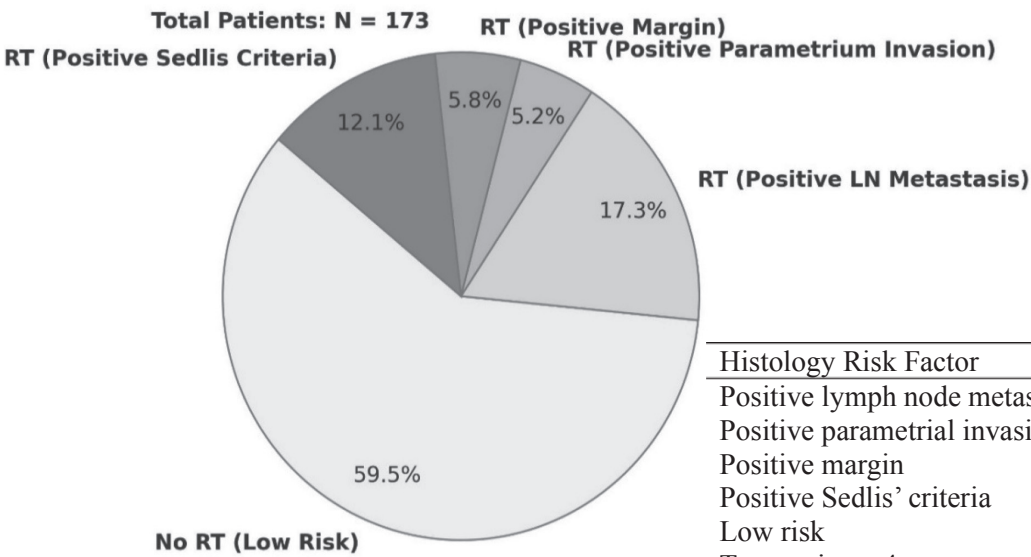
Table 1 Baseline characteristics (N=173) (con.)

Baseline characteristics	Total n (%) 173	Surgery alone n (%) 104 (60.12)	Surgery and RT n (%) 69 (39.88)	P-value
FIGO Stage (Pre-op, 2018)				**0.001**
IA1-IA2	16 (9.2)	15 (14.4)	1 (1.4)	
IB1-IB3	148 (85.6)	88 (84.6)	60 (87.0)	
IIA1-IIA2	9 (5.2)	1 (1.0)	8 (11.6)	
Recurrent rate	17 (9.8)	6 (5.8)	11 (15.9)	0.052

Abbreviations: BMI = Body mass index, LEEP = Loop electrosurgical excision procedure, SCCA = Squamous cell carcinoma, LVSI = Lymphovascular space invasion Pre-op = Pre-operative

Note: * Some patients may have had more than one symptom.

** Missing data = 61 for pre-operative LVSI due to its absence in pre-operative pathology.



Histology Risk Factor	N (%)
Positive lymph node metastasis	30 (17.3)
Positive parametrial invasion	9 (5.2)
Positive margin	10 (5.8)
Positive Sedlis' criteria	21 (12.1)
Low risk	103 (59.5)
Tumor size > 4 cm.	19 (11.0)

Figure 1 Post-operative pathological risk factor of patients (N = 173)

Figure 1 presents the postoperative histology findings used to post-operative pathological risk factor of patients. The most common indications for adjuvant radiation therapy were the presence of positive lymph node metastasis (17.3%) and positive Sedlis criteria (12.1%).

Table 2 Preoperative risk factor for adjuvant radiation therapy after radical hysterectomy in early stage cervical cancer (N = 173)

Risk factor (Pre-operative)	Surgery alone N (%)	Surgery and RT N (%)	Univariable OR (95%CI)	p-value	Multivariable aORs (95%CI)	p-value
Tumor size > 4 cm (n=28)	11 (39.3)	17 (60.7)	2.76 (1.20-6.34)	0.016	2.04 (0.80-5.17)	0.131
Non-SCCA (n=65)	37 (56.9)	28 (43.1)	1.23 (0.66-2.31)	0.506	1.14 (0.57-2.29)	0.708
Gross lesion (n=105)	57 (54.3)	48 (45.7)	1.88 (0.99-3.58)	0.053	0.94 (0.42-2.10)	0.879
Vaginal bleeding (n=85)	41 (48.2)	44 (51.8)	2.70 (1.44-5.07)	0.002	2.48 (1.21-5.06)	0.013
Suspected vaginal invasion (n=8)	1 (12.5)	7 (87.5)	11.63 (1.40-96.77)	0.023	10.92 (1.23-97.09)	0.032

Table 2 identifies preoperative risk factors for adjuvant radiation therapy after radical hysterectomy in early-stage cervical cancer. Vaginal bleeding and suspected vaginal invasion were significantly associated with the need for adjuvant radiation therapy.

In the univariable analysis, vaginal bleeding had an odds ratio (OR) of 2.70 (95% CI: 1.44-5.07; p = 0.002), while in the multivariable analysis, the adjusted odds ratio (aOR) was 2.48 (95% CI: 1.21-5.06; p = 0.013). Similarly, suspected vaginal invasion showed a strong association with adjuvant radiation therapy, with a univariable OR of 11.63 (95% CI: 1.40-96.77; p = 0.023) and a multivariable aOR of 10.92 (95% CI: 1.23-97.09; p = 0.032).

Tumor size > 4 cm was associated with an increased risk in the univariable analysis (OR 2.76; 95% CI: 1.20-6.34; p = 0.016), but this association was not statistically significant in the multivariable analysis (aOR 2.04; 95% CI: 0.80-5.17; p = 0.131).

Other factors, such as non-SCCA histology and the presence of gross lesions, indicated slightly elevated risks but did not achieve statistical significance in either analysis.

Discussion

The study found that 39.9% of patients with cervical cancer stages IA2 to IIA1 received adjuvant radiation therapy post-surgery. This percentage is comparable to other studies conducted between 1995 and 2022 that found figures between 39.5 and 39.7%.[11-13]

In this study, the primary reasons for postoperative radiation therapy were positive lymph node metastasis (17.3%) and positive Sedlis criteria (12.1%). At Lampang Hospital, preoperative evaluation was previously based on clinical staging through physical exams, without the use of CT or MRI scans. With the introduction of FIGO 2018, which incorporates imaging into staging recommendations, the use of preoperative CT or MRI has improved the accuracy of staging and facilitated better identification of stage IIICr (imaging) disease. This, in turn, reduces the likelihood of unnecessary surgery and decreases the proportion of patients requiring postoperative radiation therapy. In resource-limited areas, CT or MRI access is limited to reduce costs, so only certain patients receive scans.

In the early-stage cervical cancer usually doesn't have symptoms until it begins to spread, making it hard to detect.

Pretorius et al. determined that presentation with an abnormal Pap smear is associated with early stage and smaller tumor size, whereas presenting with symptoms other than abnormal Pap smear, such as abnormal vaginal bleeding or pain, is associated with a higher stage but not with disease-free survival.[14] Our study examines indirect factors that influence the need for adjuvant therapy after surgery, based on clinical evaluation and preoperative findings associated with higher disease spread. In our study, identified vaginal bleeding and suspected vaginal invasion were associated with the need for adjuvant radiation therapy.

In our study, preoperative physical examination identified 28 patients with a tumor size of 4 cm or larger. Only 19 individuals had tumors larger than 4 cm, as confirmed by postoperative pathology results. This suggests that the preoperative assessment of tumor size may not have been accurate enough. Pan et al. studied preoperative tumor size assessment compared to final pathology in stage IB2. Physical exams and MRI overestimated tumor size. MRI had 83.2% concordance with final pathology (2-4 cm). Physical exams showed 91.1% concordance with MRI and 80.6% concordance with final pathology.[15]

In cases where the tumor size exceeds 4 cm, it is classified as "bulky IB and IIA cervical cancer" (FIGO 2018 stage IB3 and IIA2). In the United States, where MRI is commonly used for preoperative evaluation, the NCCN (National Comprehensive Cancer Network) guidelines[16] typically recommend definitive chemoradiation over radical surgery with or without adjuvant radiation therapy. In our study, postoperative radiation therapy was administered to 17 patients (60.7%) in this group, which was significant in univariable analysis. Additionally, suspected vaginal invasion (aOR 10.92, 95% CI: 1.23–97.09) and vaginal bleeding (aOR 2.48, 95% CI: 1.21-5.06) were strongly associated with the need for adjuvant radiation therapy. These findings suggest a greater disease burden not fully detected by clinical staging. Therefore, in patients with bulky tumors, vaginal bleeding, or suspected vaginal extension, primary chemoradiation should be considered to avoid unnecessary dual-modality treatment.

Based on our findings, in areas with limited access to CT or MRI, primary radical hysterectomy may be appropriate for patients whose tumors are assessed as less than 4 cm on physical examination. However, patients should be informed that they may need adjuvant radiation therapy if other risk factors are present, like vaginal bleeding or vaginal invasion. For tumors larger than 4 cm, further evaluation with MRI or CT is advised to check for pelvic node metastasis before deciding on treatment. If imaging shows no metastasis, patients can choose either surgery or chemoradiation as their primary treatment. They were informed that surgery carries a high chance of requiring adjuvant radiation therapy, but this approach has the advantage of providing pathological staging.

In settings where advanced imaging is not routinely available, these simple clinical indicators may help guide treatment selection and reduce the likelihood of dual-modality therapy. Identifying high-risk patients before surgery allows clinicians to tailor treatment, improve patient counseling, and reduce unnecessary complications from combined therapies.

The strength of this research is that it uses data collected from a single healthcare center. Preoperative assessments and consistent treatment protocols are homogeneous. The study has limitations, including a small sample size for specific characteristics. The lack of LVSI reporting in pre-surgery pathology results (61 cases),

especially in patients with visible tumors, prevented including this important prognostic factor in the analysis. In the future, addressing these restrictions might increase the accuracy of the research.

Conclusion

The research shows that Lampang Hospital has a 39.9% postoperative radiation therapy rate after radical hysterectomy. Radiation therapy requirements cannot be predicted by preoperative clinical examinations alone. For improved treatment planning, advanced imaging like CT or MRI should be used whenever possible. In regions with limited access, evaluations should be prioritized for high-risk patients who present with vaginal bleeding, vaginal invasion, or tumor size greater than 4 cm.

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