Factors predictive of parametrial boost in patients with cervical cancer treated with definitive chemoradiation

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ARTICLE INFO	ABSTRACT
	Objective: The aim of this study is to identify demographic, clinical, and treatment-related characteristics associated with the prescription of parametrial boost (PMB) in cervical cancer patients undergoing definitive chemoradiation. *Materials/Methods:* A retrospective chart review of 132 non-metastatic cervical cancer patients treated with definitive chemoradiation from May 2017 to December 2019 was performed. Demographic, clinical, and treatment characteristics were obtained and compared between those who received PMB and those who did not. Clinical outcomes (pelvic recurrence, tumor persistence, distant metastases, and median survival time) were also gathered and compared. Statistical software was used for analysis, with a $p < 0.05$ considered statistically significant. *Results:* Of the 132 patients included in the analysis, 74 (56%) received PMB of 10 Gy in five daily fractions and 58 (44%) did not. Patients who received PMB were more likely to have pelvic sidewall invasion at the time of diagnosis (OR 4.053, 95% CI 1.163–14.13, $p < 0.05$) and received more cycles of concurrent chemotherapy during whole pelvis irradiation (OR 2.149, 95% CI 1.370–3.371, $p < 0.05$). At a median follow-up of 24 months, there was no statistically significant difference in the crude rates of pelvic recurrence, tumor persistence, distant metastasis, and median survival between the two groups. *Conclusion:* Presence of pelvic sidewall invasion at diagnosis and increased number of chemotherapy cycles were predictive of administering PMB after whole pelvis irradiation. There was no significant difference in treatment outcomes for those with and without PMB.

1. Introduction

Cervical cancer is the fourth most frequent cancer in women worldwide. (World Health Organization, 2021) In the Philippines, it ranks second only to breast cancer. (Department of Health. Uterine Cervix Cancer. Accessed July 15, 2021) Cervical cancer is managed with external beam radiotherapy (EBRT) concurrent with chemotherapy, followed by intracavitary brachytherapy (ICBT). (Motter et al., 2020) After a full course of pelvic EBRT (45–50 Gy) over 22 to 30 days, a parametrial boost (PMB) is often indicated for patients with persistent disease in the distal parametria and pelvic sidewalls. (Halperin et al., 2019) An additional 5–10 Gy is usually delivered to the parametria by EBRT since these regions are out of reach from the standard ICBT. (Mohamed et al., 2015) However, there remains little consensus as to its

indications, optimal technique, or dose.

In our institution, it is our practice to give at least five cycles of chemotherapy together with EBRT, followed by four fractions of ICBT. In between the external beam radiotherapy and brachytherapy, we have the option to give a parametrial boost if clinically indicated. It is a consensus decision made by the gynecologic oncologist and the radiation oncologist.

With the advent of modern radiotherapy techniques such as image-guided brachytherapy (IGBT) and interstitial (IS) needles, PMB may become unnecessary. (Mohamed et al., 2015; Lindegaard and Tanderup, 2012; Arya et al., 2018) Nevertheless, in low-resource and high-volume settings where cervical cancer mostly presents at locally advanced stages, PMB continues to be a relevant and useful technique.

This study aims to identify demographic, clinical, and treatment-

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related characteristics associated with the administration of PMB in cervical cancer patients treated with definitive chemoradiation.

2. Materials and methods

2.1. Patients

The authors retrospectively reviewed the records of service patients diagnosed with cervical cancer International Federation of Gynecology and Obstetrics (FIGO) 2018 Stage IB-IVA who were treated with definitive chemoradiation from May 2017 to December 2019 at the Division of Radiation Oncology, Philippine General Hospital. Patients who presented with metastatic disease, underwent surgical resection, or were treated with palliative intent were excluded from this review.

2.2. Staging

Patients were staged according to the FIGO 2018 staging criteria. (Bhatla et al., 2018) Patients diagnosed with FIGO 2009 staging criteria were re-staged. (Abu-Rustum et al., 2011) Pre-treatment evaluation included baseline internal examination performed by a gynecologic oncologist and transvaginal sonography. Metastatic work-up included chest x-ray, whole abdomen ultrasound, and alkaline phosphatase measurement. Cystoscopy or proctosigmoidoscopy with biopsy were done to confirm bladder or rectal involvement, respectively. Where indicated, further imaging with contrast-enhanced computed tomography (CT) scan of the chest, whole abdomen, or bone scintigraphy were requested. Pelvic and *para*-aortic lymph nodes were considered involved if their short-axis diameter measured ≥ 1 cm on CT scan or ultrasound. Human papilloma virus (HPV) testing was not routinely done as it was not widely available.

2.3. Whole pelvis external beam radiotherapy

Patients underwent CT simulation and were treated with a four-field or box technique using a linear accelerator or a Cobalt-60 machine. Target delineation or contouring was done on CT simulation images and included the gross primary disease, uterus, cervix, parametria, proximal vagina, and pelvic nodes starting from the bifurcation of the aorta. Extended field radiotherapy was employed at the discretion of the treating radiation oncologist for cases with prominent or enlarged *para*-aortic or pelvic nodes. The total dose was 50 Gy given in 2 Gy fractions, with some patients receiving midline shielding after 46 Gy.

2.4. Parametrial boost

PMB was indicated for patients with persistent parametrial and/or sidewall disease on the last week of whole pelvis EBRT. This was identified by the gynecologic oncologist through internal examination. An additional 10 Gy in 2 Gy fractions was given through rectangular opposing anterior-posterior fields with a standard 4-cm midline block. The superior margin was placed at the upper margin of the sacroiliac joint or the superior-most extent of the parametrial contour, whichever was higher. The inferior and lateral borders were the same as the whole pelvis EBRT field. The decision for PMB was largely dependent on the internal examination done by the gynecologic oncologist between Day 20 and 25 of EBRT.

2.5. Chemotherapy

The standard chemotherapeutic radiosensitizer was cisplatin at a dose of 40 mg/m^2. Patients with elevated creatinine received carboplatin instead. Chemotherapy was intended to be given weekly for five to six cycles. However, this was discontinued if adverse drug reaction/ toxicities developed or if the following parameters were found: absolute neutrophil count < 1,500 cells/mm^3, hemoglobin < 10 g/dL, platelet

count < 100×10^9/L, or creatinine clearance < 30 mL/min. If these parameters were corrected, chemotherapy sessions resumed. In some patients with poor kidney function (creatine clearance < 20 mL/min), radiosensitizer was omitted.

2.6. Brachytherapy

Brachytherapy was performed after completion of EBRT sessions, including PMB. This was done in patients with a central tumor size of $\leq$ 4 cm on internal examination using a cobalt-60 high dose rate brachytherapy source (SagiNova ® HDR Afterloader). X-ray based intracavitary brachytherapy was performed using Fletcher or Henschke tandem applicators, and a dose of 7 Gy was delivered to point A for every fraction, for a total of four fractions. This resulted in a cumulative equivalent dose (EQD2) of 85.7–89.7 Gy$_{10}$. In cases of inadequate EBRT response (i.e., central tumor size of > 4 cm), institutional practice was to initiate systemic therapy (carboplatin-paclitaxel) every three weeks prior to brachytherapy. Reassessment was done after every cycle for tumor downstaging and brachytherapy eligibility.

2.7. Predictive factors and outcomes analyzed

Patients were classified into either of two groups: 1) those who received PMB or 2) those who did not.

Demographic, clinical, and treatment-related information was then gathered. Demographic characteristics included age, pretreatment hemoglobin, body mass index (BMI), and smoking history.

Tumor characteristics included histology, 2018 FIGO stage at diagnosis, greatest tumor dimension as determined by internal examination or imaging, presence of parametrial invasion, presence of pelvic sidewall invasion, pelvic nodal status, and *para*-aortic lymph node status. Pelvic and *para*-aortic lymph node status was classified as enlarged ($\geq$1 cm), prominent (<1cm), or none.

Treatment-related characteristics included diagnosis to treatment interval, external beam radiotherapy (EBRT) machine used, length of EBRT treatment, type of chemotherapy given, number of cycles of concurrent chemotherapy, utilization of midline shielding, and occurrence of treatment breaks. The time at diagnosis was specified as the date when patients were first seen and examined in the subspecialty clinic of Gynecologic Oncology. At our institution, only histologically confirmed cases are referred to Gynecologic Oncology. Work-up may not have been necessarily completed during this time.

Parameters such as pelvic recurrence, central tumor persistence, distant metastases, and survival were also recorded.

2.8. Statistical methods and data analysis

A treatment break was defined as any single break in radiation treatment $\geq$ 3 days excluding weekends or holidays or multiple breaks during radiotherapy resulting in $\geq$ 5 days of missed treatment. (Zaki et al., 2016) Pelvic recurrence was defined as presence of pelvic disease (histologically proven cervical, vaginal, or vulvar recurrence) and/or lymph nodes with a short axis diameter of $\geq$ 1.0 cm detected on subsequent follow-up imaging for patients who demonstrated no evidence of disease at initial follow-up. Central tumor persistence was defined as presence of tumor with no significant decrease in size from baseline after initial whole pelvis EBRT with concurrent chemotherapy. For this study, it was defined as a tumor size of > 4 cm on internal examination done during the last week of EBRT or after its completion. Distant metastasis was defined as presence of visceral or osseous metastasis detected on follow-up imaging. Survival time was defined as interval between last day of EBRT and date of death or last follow-up.

Descriptive statistics were used to summarize the demographic, clinical, and treatment-related characteristics of patients. Odds ratio and corresponding 95% confidence intervals from binary logistic regression were computed to determine significant predictors of parametrial boost.

All statistical tests were two-tailed tests. Shapiro-Wilk was used to test the normality of the continuous variables. Missing values were not replaced or estimated. Null hypotheses were rejected at 0.05 α-level of significance. STATA 13.1 was used for data analysis.

3. Results

3.1. Demographic, clinical, and treatment-related characteristics

Of 132 patients eligible for analysis, 74 (56%) received PMB while 58 (44%) did not. Table 1 shows the demographic, clinical, and treatment-related characteristics of patients included in the analysis. The mean age at diagnosis was 47 years old and ranged from 35 to 58 years old. Mean pre-treatment hemoglobin level was 12 g/dL (range: 10.7 g/dL – 13.1 g/dL). Majority were considered overweight, as per the WHO Asian BMI cut point, (Jih et al., 2014) with a mean BMI of 24.6 kg/m^2, and most had no history of smoking (77%). Most cancers were Stage IIIA-IVA (65.9%) and squamous cell carcinoma in histology (72%). Mean tumor diameter was 6 cm, and parametrial and pelvic sidewall invasion at diagnosis were observed in 90.9% and 51.5%, respectively. Majority also had no or just prominent pelvic (59.8%) and *para*-aortic (87.1%) lymph nodes.

For treatment, a cobalt-60 machine was used in 63.6% of patients while a linear accelerator was used in 36.4%. Treatment interruptions were noted in 42.4% mostly due to abnormal hemoglobin levels. For these patients, treatment was reinstated once blood transfusion was completed. The mean number of chemotherapy cycles was four, with 86.4% receiving cisplatin. Despite a planned 25 treatment days over a period of 33 days, the mean EBRT treatment duration was 47 days. All patients also had a treatment delay of at least 36 days (mean: 100 days), raising concern that the stage at diagnosis may not be the same as that at the start of treatment.

Interestingly, it was found that more than half of patients (53.3%) with Stage IB-IIB disease received 5–6 cycles of chemotherapy, whereas, more than half of patients (55.2%) with higher stage disease (IIIA-IVA) received less chemotherapy (≤4 cycles) (Table 2). It was additionally found that 68.6% of patients with central tumor persistence after pelvic EBRT received fewer cycles of chemotherapy. On the other hand, most patients without central tumor persistence (53.6%) counterintuitively received more chemotherapy (5–6 cycles).

The results show that more patients with higher stage (59.8%) and central tumor persistence (65.7%) had longer EBRT treatment durations of 40 days or longer (Table 3).

3.2. Factors associated with parametrial boost

Results of the binary logistic regression analysis are reported in Table 4. This revealed that patients were more likely to be treated with PMB if they had pelvic sidewall invasion at the time of diagnosis, which may be detected either clinically through internal examination or radiologically through transvaginal sonography (OR 4.053, 95% CI 1.163–14.13, p < 0.05) and had increased number of concurrent chemotherapy cycles (OR 2.149, 95% CI 1.370–3.371, p < 0.05). Of note, increased EBRT treatment length also showed a trend toward statistical significance (OR 0.965, 95% CI 0.931–1.001, p = 0.054).

3.3. Treatment outcomes

At a median follow-up of 24 months, there was no statistically significant difference in the evaluated treatment outcomes for crude rates of pelvic recurrence (6.8% vs. 10.3%), central tumor persistence (29.7% vs. 22.4%), distant metastases (6.8% vs. 6.9%), and median survival (240 days vs. 332 days, p = 0.3685) (Table 5).

Impact of PMB on treatment outcomes of patients with pelvic sidewall involvement and enlarged pelvic nodes at diagnosis was also evaluated revealing no significant differences in crude rates of pelvic

Table 1

Demographic, clinical, and treatment-related characteristics of cervical patients treated with definitive chemoradiation (n = 132).

	Total Patient Population n (%)	Parametral Boost n (%)		p-value
		With (n = 74) n (%)	Without (n = 58) n (%)	
Age (mean ± SD)	47.21 ± 10.99	46.85 ± 11.37	47.67 ± 10.58	0.6719
Pretreatment hemoglobin (mean ± SD)	12 ± 1.31	12.06 ± 1.40	11.92 ± 1.21	0.5501
BMI (mean ± SD)	24.62 ± 3.99	24.58 ± 3.84	24.67 ± 4.19	0.8936
Smoking history				0.518
Yes	28 (21.2)	14 (18.9)	14 (24.1)	
No	102 (77.3)	58 (78.4)	44 (75.9)	
Histology				0.343
Squamous cell carcinoma	95 (72)	57 (77)	38 (65.5)	
Adenocarcinoma	22 (16.7)	10 (13.5)	12 (20.7)	
Others	15 (11.4)	7 (9.5)	8 (13.8)	
2018 FIGO Stage				0.021*
IB-IIB	45 (34.1)	19 (25.7)	26 (44.8)	
IIIA-IVA	87 (65.9)	55 (74.3)	32 (55.2)	
Greatest tumor diameter (mean ± SD)				
IE	5.95 ± 1.61	6.08 ± 1.44	5.79 ± 1.8	0.3093
Imaging	5.54 ± 1.77	5.6 ± 1.68	5.46 ± 1.88	0.6577
Presence of parametrial invasion				0.001*
Yes	120 (90.9)	73 (98.6)	47 (81)	
No	12 (9.1)	1 (1.4)	11 (19)	
Presence of pelvic side wall invasion				0.002*
Yes	68 (51.5)	47 (63.5)	21 (36.2)	
No	64 (48.5)	27 (36.5)	37 (63.8)	
Pelvic node status				0.32
Enlarged	51 (38.6)	31 (41.9)	20 (34.5)	
None or Prominent	79 (59.8)	41 (55.4)	38 (65.5)	
Paraaortic lymph node status				0.702
Enlarged	15 (11.4)	9 (12.2)	6 (10.3)	
None or Prominent	115 (87.1)	63 (85.1)	52 (89.7)	
ERBT dose (mean ± SD)	50.04 ± 0.39	50.07 ± 0.54	50 ± 0.00	0.2978
Midline shielding				0.84
Yes	109 (82.6)	62 (83.8)	47 (81)	
No	22 (16.7)	12 (16.2)	10 (17.2)	
EBRT machine used				0.974
Cobalt	84 (63.6)	47 (63.5)	37 (63.8)	
LINAC	48 (36.4)	27 (36.5)	21 (36.2)	
Presence of treatment breaks				0.119
Yes	56 (42.4)	27 (36.5)	29 (50)	
No	76 (57.6)	47 (63.5)	29 (50)	
Type of chemotherapy given				0.642
Cisplatin	114 (86.4)	63 (85.1)	51 (87.9)	
Carboplatin, Others, None	18 (13.6)	11 (14.9)	7 (12.1)	
Number of cycles of concurrent chemotherapy (mean ± SD)	4.35 ± 1.24	4.59 ± 0.93	4.03 ± 1.49	0.0092*
Diagnosis to treatment interval length (mean ± SD)	100.11 ± 64.82	101.85 ± 68.02	97.86 ± 60.93	0.7282

recurrence (5.4% vs. 10%), central tumor persistence (35.7% vs. 23.3%), distant metastases (7.1% vs. 10%), and median survival (224 days vs. 332 days, p = 0.0953) (Table 6).

Table 2

Comparison of clinical characteristics and outcomes according to number of cycles of concurrent chemotherapy.

	Number of Chemotherapy Cycles		p-value
	5 to 6 cycles	4 or less cycles	
	n (%)	n (%)	
Stage			0.354
IB - IIB	24 (18.2)	21 (15.9)	
IIIA - IVA	39 (29.5)	48 (36.4)	
Pelvic side wall invasion			0.228
Yes	29 (22)	39 (29.5)	
No	34 (25.8)	30 (22.7)	
Central tumor persistence			0.024*
Yes	11 (8.3)	24 (18.2)	
No	52 (39.4)	45 (34.1)	

*p-value < α = 0.05

Table 3

Comparison of clinical characteristics and outcomes according to EBRT treatment duration.

	EBRT Treatment Duration		p-value
	40 days or more	39 days or less	
	n (%)	n (%)	
Stage			0.232
IB - IIB	22 (16.7)	0.354	
IIIA - IVA	52 (39.4)		
Pelvic side wall invasion		0.228	0.51
Yes	40 (30.3)	28 (21.2)	
No	34 (25.8)	30 (22.7)	
Central tumor persistence		0.024*	0.179
Yes	23 (17.4)	12 (9.1)	
No	51 (38.6)	46 (34.8)	

4. Discussion

In this study, it was found that the prescription of a parametrial boost was associated with having pelvic sidewall involvement at diagnosis and more cycles of concurrent chemotherapy. The variables evaluated for prediction of parametrial boost in this study are prognostic factors for cervical cancer and also predictors of treatment effect of the initial concurrent chemotherapy and whole pelvis EBRT. (Zaki et al., 2016; Quinn et al., 2019; Mayadev et al., 2018; Vinh-Hung et al., 2007; Yan et al., 2019; Wagner et al., 2011; Yan et al., 2019; Treharne et al., 2014; Nugent et al., 2010) The need for additional PMB is, thus, a surrogate measure of persistent peripheral disease requiring higher dose for disease eradication.

Patients with pelvic sidewall invasion (at least Stage IIIB) at the time of diagnosis were four times more likely to be prescribed PMB compared to those without pelvic sidewall invasion. It is easy to understand why. The pelvic sidewalls usually only receive 10–30% of the dose per fraction of intracavitary brachytherapy. (Viswanathan et al., 2012) This results in disparate doses received in the parametrium and the central tumor, which is not a problem for patients with only central disease. To correct this, persistent sidewall disease compels boosting by EBRT. Regardless of pre-treatment status, all patients are re-evaluated one week before the end of external beam radiotherapy, to get a good picture of patient response. Our results say that these patients with advanced stage disease still do need parametrial boost even if they were near completion of external beam radiotherapy.

While presence of pelvic sidewall invasion is commonly cited as an indication for PMB, another indication is the presence of pelvic nodes, (Viswanathan and Thomadsen, 2012) which may be encompassed within the treatment field. However, this did not show statistical significance in our study. An observed limitation in our practice is the reliance on internal examination alone, without the benefit of imaging,

Table 4

Binary logistic regression analysis for likelihood of receiving PMB.

Variable	Adjusted Model		
	Odds Ratio	**95% CI**	**p-value**
Age	1.004	0.958, 1.052	0.87
Pretreatment hemoglobin	1.292	0.905, 1.846	0.158
BMI	1.016	0.907, 1.138	0.783
Smoking history			
No (reference)			
Yes	1.072	0.374, 3.072	0.897
Histology			
Squamous cell carcinoma (reference)			
Adenocarcinoma	0.403	0.110, 1.475	0.17
Others	0.579	0.152, 2.211	0.424
2018 FIGO Stage			
IB - IIB (reference)			
IIIA - IVA	1.594	0.339, 7.482	0.555
Greatest tumor diameter by Imaging	0.977	0.729, 1.308	0.874
Presence of pelvic side wall invasion			
No (reference)			
Yes, unilateral/bilateral	4.053**	1.163, 14.13	0.028
Pelvic node status			
None or Prominent (reference)			
Enlarged	1.319	0.375, 4.648	0.666
Paraaortic lymph node status			
None or Prominent (reference)			
Enlarged	1.868	0.340, 10.26	0.472
Midline shielding			
No (reference)			
Yes	1.004	0.301, 3.348	0.995
EBRT machine used			
Cobalt (reference)			
LINAC	1.337	0.476, 3.753	0.581
EBRT treatment length	0.965*	0.931, 1.001	0.0572
Presence of treatment breaks			
No (reference)			
Yes	1.084	0.336, 3.498	0.892
Type of chemotherapy given			
Cisplatin (reference)			
Carboplatin, Others, or None	2.721	0.533, 13.88	0.229
Number of cycles of concurrent chemotherapy	2.149***	1.370, 3.371	0.000867
Diagnosis to treatment interval length	1.004	0.997, 1.011	0.289

*** p < 0.01, ** p < 0.05, * p < 0.1

Presence of parametrial invasion at diagnosis was excluded as a variable due to the rare event that patients without parametrial invasion at diagnosis will receive PMB.

to assess indications for PMB. This may miss the detection of peripheral disease located more superiorly and may fail to document treatment response to the gross nodes. The use of MRI would help in evaluating presence of residual peripheral disease that may benefit with additional treatment.

Another limitation in our practice is the use of conventional techniques in treating those with grossly enlarged nodes. Many patients are constrained to treatment with 2D or 3D external beam techniques and x-ray-based brachytherapy. With more sophisticated methods such as

Table 5
Treatment outcomes of patients treated with cervical cancer.

	Total n (%)	Parametrial Boost		p-value
		With (n = 74) n (%)	Without (n = 58) n (%)	
Recurrence	11 (8.3)	5 (6.8)	6 (10.3)	0.604
Persistence	35 (26.5)	22 (29.7)	13 (22.4)	
Distant Metastasis	9 (6.8)	5 (6.8)	4 (6.9)	
Last day of EBRT to Last follow-up interval length (median survival time, days)	291	240	332	0.3685

Table 6
Treatment outcomes of patients with pelvic sidewall involvement and pelvic lymphadenopathy at diagnosis.

	Total n (%)	Parametrial Boost		p-value
		With (n = 56) n (%)	Without (n = 30) n (%)	
Recurrence	6 (7)	3 (5.4)	3 (10)	0.463
Persistence	27 (31.4)	20 (35.7)	7 (23.3)	
Distant Metastasis	7 (8.1)	4 (7.1)	3 (10)	
Last day of EBRT to Last follow-up interval length (median survival time, days)	249	224	332	0.0953

intensity modulated radiotherapy (IMRT) and image-guided brachytherapy, dose escalation is feasible with fewer toxicities. (Dang et al., 2019)

An unanticipated result of this study is the higher likelihood of receiving PMB among patients who had previously received more cycles of concurrent chemotherapy. Published evidence shows that as more cycles of chemotherapy are given concurrently with EBRT, a more obvious treatment response is expected, (Nugent et al., 2010) making PMB less warranted. Theoretically, more chemotherapy should yield better results.

In our study, however, patients who presented with more advanced stage received fewer cycles of chemotherapy (4 or less out of a planned 5 cycles) and had higher rates of central tumor persistence.

Upon review, it was found that not all our patients received the ideal number of chemotherapy cycles as a result of adverse drug reactions, toxicities, unacceptable hematologic parameters, or declining renal function. It was possible that patients with early-stage and limited disease were able to receive more cycles of chemotherapy because they were less predisposed to conditions that could preclude its administration such as anemia from bleeding or decreased renal function from obstructive uropathy. This also likely led to lower rates of persistent central disease and subsequent treatment with PMB for the remaining peripheral disease. On the other hand, most patients with advanced disease and central tumor persistence did not proceed with further local treatment, including ICBT, and were treated with systemic chemotherapy instead (n = 21/35). In our institution, patients with central tumor persistence after pelvic EBRT were treated with systemic chemotherapy before proceeding with ICBT.

This observed pattern involving stage and chemotherapy cycles was also observed in a retrospective study done by Escande et al wherein patients with more advanced FIGO stage received fewer cycles of chemotherapy (≤4 cycles) in comparison to those with early-stage disease who received 5–6 cycles. Patients who received fewer cycles of chemotherapy also had poorer outcomes in terms of locoregional control and survival(Escande et al. 2020)

Another unexpected result of this study is the association of longer

EBRT treatment with less likelihood of PMB, exhibiting a trend toward statistical significance.

Our results showed that for every increase of one day in EBRT treatment length, the odds of undergoing PMB decreased by 3.5%. In cervical cancer, overall treatment time is crucial as improved local control and survival are achieved when EBRT and brachytherapy are completed in less than eight weeks. (Viswanathan and Thomadsen, 2012) There is also accelerated repopulation of tumor in protracted treatment. (Huang et al., 2012) As a result, we expected patients with longer EBRT treatment duration to respond less to EBRT, thereby requiring PMB. A possible explanation for our results would be that patients with more advanced disease or central tumor persistence had other conditions that precluded continuous treatment—anemia, weakness, or other similar conditions. Majority of these patients did not proceed with brachytherapy either and were likely treated with systemic therapy instead.

Differences in treatment outcomes for those who did and did not receive PMB did not reach statistical significance in terms of pelvic recurrence, central tumor persistence, distant metastases, and median survival. This suggests that PMB itself is not predictive of oncologic outcomes and that these are likely still influenced by persistence of central, rather than peripheral, disease. In a retrospective analysis by Liu et al, patients with persistent central disease were found to have poor treatment outcomes with a 2-year survival rate of 21.7% and a median survival of 17 months. (Liu et al., 2013)

5. Conclusion

Presence of pelvic sidewall invasion at diagnosis and increased number of previous chemotherapy cycles were predictive of administering PMB after whole pelvis irradiation. There was no significant difference in treatment outcomes for those with and without PMB. This was despite the fact that most patients treated with PMB had more high-risk features (i.e., higher stage, presence of parametrial and pelvic side wall invasion at diagnosis).

The validity of this study is limited by its retrospective nature, short follow-up period, and small sample size due to high rates of attrition. Indications for PMB remain uncertain and will remain so until randomized controlled trials are undertaken, specifically of patients with Stages IIB and IIIB-C1.

Nonetheless, the use of PMB remains an option in low-resource and high-volume centers, just as in our institution. Until better regimens are developed, PMB will still be one of the available modalities for optimizing radiation doses for cervical cancer patients.

Author contribution

JC conceptualized the research goals and aims. KJ developed and designed the protocol and methodology and accomplished data collection. JC was responsible for oversight of the research planning and execution. KJ wrote the original draft. JC reviewed and edited the final paper.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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