

Outcomes and patterns of management of metastatic/recurrent cervical carcinoma in Malaysia: A single institutional observational cohort study

Siti Mariam Yacob, (MCO)¹, Rozita Abdul Malik, (MCO)²

¹Department of Nuclear Medicine, Radiotherapy and Oncology, Universiti Sains Malaysia, Campus of Health Science, Kelantan, Malaysia, ²Department of Clinical Oncology, Universiti Malaya, Kuala Lumpur, Malaysia

ABSTRACT

Introduction: Cervical cancer is the fourth most common malignancy in women. Approximately 15% of the patients have metastatic disease. The Malaysian National Cancer Registry (MNCR) 2017-2021 reported that over the five-year period, there were 2654 new cases. 47.1% of the patients presented with late stages (stages 3 and 4), slightly higher compared to 41% in the MNCR 2012-2016 report. There were no standard approaches to the management of metastatic/recurrent cervical cancer. Therefore, this study aimed to determine the survival outcomes of patients with metastatic/recurrent cervical cancer and to evaluate the clinicopathological factors based on demographic and tumour characteristics that may affect survival outcomes. Besides that, we would like to outline the management patterns in this cohort of patients.

Materials and Methods: This was a retrospective observational cohort study looking at the 35 patients diagnosed with metastatic/recurrent cervical cancer at the Department of Clinical Oncology, Universiti Malaya Medical Centre (UMMC) over the five-year period from 1st of January 2016 until 31st of December 2020. Data were obtained from the electronic medical record. The Kruskal-Wallis H and Mann-Whitney U non-parametric tests, Spearman correlation, and Kaplan-Meier survival analysis were conducted to analyse the survival outcomes and clinicopathological factors that may affect the survival outcomes in the form of progression-free survival (PFS) and overall survival (OS). Descriptive analysis was used to describe the prevalence of metastatic/recurrent cervical cancer and the patterns of management.

Results: Out of the total 94 cervical cancer patients registered at the Department of Clinical Oncology, UMMC, 37.2% had metastatic/recurrent disease. Survival analysis demonstrated that median PFS and OS for metastatic/recurrent cervical cancer were six and 12 months, respectively, which were consistent with the global populations. Nonparametric multivariate tests and survival analysis showed that the presence of metastatic disease at less common sites had worse survival. Most of the patients received active oncological treatments, i.e., chemotherapy, radiotherapy or combinations of both.

Conclusion: This study showed that a significant portion of the patients were diagnosed at a late stage, with poor survival outcomes, indicating the necessity for enhanced

initiatives in the screening and education programmes to increase awareness of early diagnosis and detection, hence improving survival outcomes of cervical cancer patients.

KEYWORDS:

Cervical cancer, metastatic cervical cancer, recurrent cervical cancer, survival outcomes

INTRODUCTION

Carcinoma of the cervix is one of the most common malignancies in the world. According to the Global Cancer (GLOBOCAN) 2022 report, an estimated 661,021 cervical cancer cases were reported globally, currently ranked the fourth most common cause of cancer-related mortality among women, with 348,189 deaths.¹ In addition, the symptoms, particularly pelvic pain and per-vaginal bleeding, can result in significant morbidities for the patients, leading to hospitalisation, blood transfusion, reduced performance status, and ultimately affecting their quality of life.

The Papanicolaou (PAP) smear screening programme has significantly contributed to early detection of cervical cancer, particularly in developed countries. However, it remains a challenge in developing countries, as we still observe higher incidence and mortality rates. Developed or wealthier countries such as New Zealand, Canada, and Saudi Arabia showed that their mortality from cervical cancer was seven times lower compared to poorer countries such as Sub-Saharan Africa, which reported 18 times higher mortality rates.²

The high mortality from cervical cancer is primarily due to the late diagnosis at the advanced stage. About 13% of the patients presented with metastatic disease worldwide.³ Despite the small percentage, studies showed that five-year survival rates dropped from 91.5% for localised disease to only 16.5% for metastatic disease.³

The radical treatment for localised disease would consist of either surgical resection, including lymphadenectomy, and/or radiation therapy with or without chemotherapy, depending on the staging.⁴ However, in metastatic/recurrent disease, the best treatment modalities are still an ongoing dilemma. Therefore, it is interesting to study current evidence and updates on the management of metastatic/recurrent cervical cancer.

This article was accepted: 17 July 2026

Corresponding Author: Rozita Abdul Malik

Email: rozita@ummc.edu.my

MATERIALS AND METHODS

This was a retrospective single-centre study conducted at Universiti Malaya Medical Centre (UMMC), a tertiary oncology referral centre in Malaysia. Patients diagnosed with metastatic/recurrent cervical carcinoma, either de novo metastatic disease or recurrent disease not amenable to curative treatment, who were registered and treated at the Department of Clinical Oncology between 1 January 2016 and 31 December 2020 were included. All histological subtypes were eligible. Patients who received only radiotherapy at UMMC but continued systemic treatment and follow-up at other centres were excluded.

Patients were identified through departmental registry records. Demographic, clinicopathological, and treatment-related data were extracted from electronic medical records using a standardised proforma. Survival status and dates of death were obtained from the Malaysian National Institute of Health registry using national identification numbers.

The primary outcomes were progression-free survival (PFS) and overall survival (OS), defined as the time from diagnosis of metastatic or recurrent disease to disease progression or death, and to death from any cause, respectively. Demographic factors (age, ethnicity, performance status, and comorbidities), tumour characteristics (disease status at diagnosis, histology, and metastatic sites), and first-line treatment modalities were analysed.

Descriptive statistics were used to summarise patient characteristics, treatment patterns, and prevalence of metastatic/recurrent cervical carcinoma. Normality of survival data was assessed using the Shapiro–Wilk test. As PFS and OS were not normally distributed, non-parametric tests were applied. The Mann–Whitney U test and Kruskal–Wallis H test were used to evaluate differences in survival outcomes across clinicopathological variables. Kaplan–Meier survival analysis was performed for survival estimation, and Spearman’s rho was used to assess correlations between survival outcomes and clinical variables. A p-value < 0.05 was considered statistically significant. The data cut-off date was 1st of June 2025.

Ethics approval was obtained from the Medical Research Ethics Committee (MREC ID: 202315-11924). Individual informed consent was waived due to the retrospective nature of the study.

RESULTS

Prevalence of metastatic cervical carcinoma

During the period from 1st of January 2016 until 31st of December 2020, a total of 94 cervical cancer patients were registered at the Department of Clinical Oncology, UMMC. Out of this, 35 patients (37.2%) were found to have metastatic or recurrent diseases that were not amenable to curative treatment.

Demographic factors

In this study, the age of the patients was grouped based on the MNCR as a guide. The distribution of patients revealed significant prevalence among middle-aged individuals.

60.2% of the patients were observed to be in the age group between 40 and 64 years old.

Ethnicity played a notable role in the distribution of metastatic/recurrent cervical carcinoma within the study population. The Chinese ethnic group represented the majority of the patients, accounting for 68.6% of the sample, followed by the Malay group with 25.7% and the Indian group with 5.7%.

Eastern Cooperative Oncology Group (ECOG) performance status scoring was used to determine patients’ performance status. 94.4% of the patients had good performance status with an ECOG score of less than 2.

The prevalence of comorbidities in this cohort of patients revealed that most of the patients did not have existing medical illnesses. Among those with comorbidities, hypertension (HPT) was the most common chronic illness (a total of 28.5%), followed by hypercholesterolaemia (HCT) (a total of 14.3%) and diabetes mellitus (DM) (a total of 11.4%). 11.4% of patients had multiple comorbidities. Table I showed the descriptive analysis for the demographic factors and tumour characteristics.

Tumour characteristics

As shown in Table I, the distribution of cancer status at initial diagnosis indicated that most of the patients (68.6%) developed metastatic or recurrent disease as a progression from previously diagnosed and treated early-stage cervical carcinoma. In contrast, only 31.4% of patients were diagnosed with de novo metastatic cervical carcinoma.

The histological subtypes of cervical carcinoma in this study demonstrated that 68.6% of cases were SCC, followed by adenocarcinoma, which accounted for 28.6% of the sample. Only one patient had a rarer neuroendocrine subtype.

For the metastatic sites’ analysis, more than 50% of the patients reported metastasis at a single site, and 48.6% of the patients had metastases at multiple sites. The data showed that nodal and local recurrence were the main disease burdens in the majority of the patients, with 45.7% and 37.1% of the patients had nodal and local recurrence, respectively. Nevertheless, lung was the most common site for visceral metastases.

Overall survival outcomes

The progression-free survival (PFS), defined as the time from the diagnosis of metastatic or recurrent diseases to the disease progression or death, whichever came first, had a median value of six months with an interquartile range (IQR) of 6.5 months. On the other hand, overall survival (OS), defined as the time from the diagnosis of metastatic or recurrent diseases to the death of the patients from any cause, had a median survival of 12 months with an IQR of 11.5 months. Two patients had not progressed and were still alive at the time of data cut-off analysis.

In addition, the Spearman’s rho correlation coefficients were calculated to assess the relationships between PFS and OS. The correlation between PFS and OS was found to be

Table I: Descriptive analysis for demographic factors and tumour characteristics

Factors	Group	N (35)	Percentage (%)
Age	20-24	1	2.9
	30-34	3	8.5
	35-39	1	2.9
	40-49	6	17.2
	50-54	1	2.9
	55-59	8	22.9
	60-64	6	17.2
	65-69	3	8.5
	70-74	3	8.5
	75+	3	8.5
Ethnicity	Malay	9	25.7
	Chinese	24	68.6
	Indian	2	5.7
ECOG	0	22	62.9
	1	11	31.5
	2	1	2.8
	3	1	2.8
Comorbidities*	No	21	60.0
	HPT	6	17.1
	DM	2	5.7
	HCT	1	2.9
	CKD	1	2.9
	HPT+HCT	2	5.7
	HPT+HCT+DM	2	5.7
Tumour characteristics			
Cancer status at initial diagnosis	Localised disease	24	68.6
	Metastatic disease	11	31.4
Histology subtype	SCC	24	68.6
	Adenocarcinoma	10	28.6
	Neuroendocrine	1	2.8
Number of metastatic/recurrence sites	1	18	51.4
	2	16	45.7
	3	1	2.9
Metastatic/recurrence site Lung	Yes	9	25.7
	No	26	74.3
Liver	Yes	3	8.6
	No	32	91.4
Bone	Yes	7	20.0
	No	28	80.0
Local recurrence	Yes	13	37.1
	No	22	62.9
Nodal	Yes	16	45.7
	No	19	54.3
Others	Yes	4	11.4
	No	31	88.6

* HPT-hypertension, DM-diabetes mellitus, HCT - hypercholesterolaemia, CKD-chronic kidney disease

statistically significant with a moderate positive correlation ($r=0.630$, $p<0.01$). This indicated that a patient who experienced a longer PFS tended to have a longer OS.

Effects of demographic factors on survival outcomes

The Kruskal-Wallis H non-parametric test revealed a statistically significant difference in progression-free survival across different age groups, with a p-value of 0.026. The median PFS varied with patients aged 60-64 years showing a much higher median of 35.50 months, while younger patients showed median PFS ranging from two to six months. Therefore, Spearman's rho correlation analysis was conducted. The correlation between PFS and age was moderate and positive ($r=0.469$, $p<0.01$); hence, this relationship was also statistically significant. These results suggested that age may play a role in the rate of disease

progression, with older patients experiencing slower progression compared to younger patients. However, the effects of different age groups were not statistically different for overall survival with a p-value of 0.158.

The Kruskal-Wallis H test also demonstrated no statistically significant differences affecting both PFS and OS between the groups in terms of ethnicity, performance status, and comorbidities, as shown in Table II. The p-values were above the threshold level of 0.05.

Effects of tumour characteristics on survival outcomes

The Mann-Whitney U non-parametric test (Table III) revealed no significant differences in PFS or OS among patients with metastases at common sites such as the lung, liver, bone, lymph nodes, or with local recurrence. However,

Table II: Kruskal-Wallis H non-parametric test for survival outcomes by demographic factors and tumour characteristics

Factors	Group	Progression free survival						Overall survival									
		N	Median	IQR	Mean Rank	Kruskal-Wallis H	p-value	Median	IQR	Mean Rank	Kruskal-Wallis H	p-value					
Demographic factors Age	20-24	1	5.00		10	20.33	0.026*	11.00		13.00	14.34	0.158					
	30-34	3	4.00	3	6.83			11.00	22	15.67							
	35-39	1	6.00		16.5			15.00		20.50							
	40-49	6	6.00	2.5	14.67			12.00	17	17.67							
	50-54	1	2.00		4			2.00		3.00							
	55-59	8	6.00	2.25	15.44			8.50	9	10.88							
	60-64	6	35.50	62.5	31.83			36.00	48	28.83							
	65-69	3	16.00	12	28.17			20.00	29	23.33							
	70-74	3	7.00	8	17.25			23.00	8	27.50							
Ethnicity	75+	3	8.00	7	20.17	1.18	0.554	12.00	13	16.00	1.17	0.558					
	Malay	9	5.00	16.5	16.44			9.00	24.75	14.56							
	Chinese	24	6.00	5.5	19.32			13.00	9.5	18.69							
ECOG	Indian	2	20.00	35	24	0.946	0.814	11.00	22.75	15.00	1.97	0.579					
	0	22	6.00	8.25	18.65			11.00	12.5	15.83							
	1	11	6.00	6	19.09			15.00	11	19.91							
	2	1	6.00		16.50			12.00		17.50							
Comorbidities	3	1	12.00		29.00	12.756	0.078	19.00		26.00	6.42	0.378					
	No	21	5.50	3	13.52			11.00	9.25	14.5							
	HPT	6	16.00	17	26.6			18.00	28.5	22.5							
	DM	2	6.50	4.25	18.75			33.00	39.5	21.75							
	HCT	1	8.00		23			9.00		10.5							
	CKD	1	12.00		28			19.00		26							
	HPT+HCT	2	6.00	5	16.5			15.00		21.5							
Tumour characteristics	HPT+HCT+DM	2	9.00		25.5	3.12	0.21	21.00		28	2.20	0.333					
	FIGO stage at initial diagnosis	Early stages (Recurrences)	24	6.00	3.75			17.46	11.50	6.5			16.14				
		Metastatic disease at presentation	11	6.00	3			20.18	16.50	37.75			18.70				
	Histology subtype	Adenocarcinoma	10	6.00	6			17.32	0.48	0.788			17.50	18.5	21.90	3.13	0.209
		Neuroendocrine	1	6.00				16.5					15.00		21.50		
		SCC	24	7.00	9			19.84					12.00	12	15.41		
	Number of metastatic sites	1	18	8.00	7			19.42	0.73	0.694			12.00	13	16.92	2.00	0.368
		2	16	6.00	9			19.06					12.00	16	19.03		
		3	1	5.00				10					5.00		5.00		

* Significant, p<0.05

Table III: Mann-Whitney U non-parametric test for survival outcomes by different metastatic sites

Metastatic site	Progression free survival						Overall survival							
	Group	N	Median	IQR	Mean Rank	Sum of Ranks	Mann-Whitney U	p-value	Median	IQR	Mean Rank	Sum of Ranks	Mann-Whitney U	p-value
Lung	Yes	9	6.00	3.00	17.90	179.00	124.00	0.705	11.00	4.50	15.28	137.50	92.50	0.434
	No	26	6.00	7.00	19.41	524.00			14.00	6.50	18.30	457.50		
Liver	Yes	3	5.00	46.00	15.75	63.00	53.00	0.522	21.00	35.25	24.88	99.50	30.50	0.114
	No	32	6.00	5.50	19.39	640.00			12.00	6.25	16.52	495.50		
Bone	Yes	7	6.00	23.75	18.88	151.00	115.00	0.97	11.00	4.00	16.36	114.50	86.50	0.733
	No	28	6.00	5.50	19.03	552.00			12.00	8.00	17.80	480.50		
Local recurrence	Yes	13	7.50	4.75	19.82	277.50	149.50	0.717	14.00	6.25	17.68	247.50	137.50	0.93
	No	22	6.00	6.00	18.50	425.50			12.00	6.00	17.38	347.50		
Nodal	Yes	16	6.00	8.50	20.59	350.00	143.00	0.407	14.50	14.75	20.04	280.50	104.50	0.213
	No	19	6.50	2.50	17.65	353.00			11.50	6.00	15.73	314.50		
Others	Yes	4	4.00	1.50	7.63	30.50	20.50	0.025*	7.50	6.50	10.25	41.00	31.00	0.121
	No	31	7.00	5.50	20.38	672.50			12.00	8.25	18.47	554.00		

*Significant, p<0.05

Table IV: Patterns of management in metastatic/recurrent cervical carcinoma

Patterns of management			N (35)	Percentage (%)
Treatment Modalities	Radiotherapy	Yes	20	57.1
		No	15	42.9
	Chemotherapy	Yes	24	68.6
		No	11	31.4
	Surgery	Yes	4	11.4
		No	31	88.6
Patterns				
	Best supportive care		6	17.1
	Chemotherapy alone		8	22.8
	Chemotherapy followed by radical RT		8	22.8
	Chemotherapy followed by palliative RT		2	5.7
	Radical RT alone		3	8.6
	Palliative RT alone		1	2.9
	Radical RT then chemotherapy		2	5.7
	Palliative RT then chemotherapy		1	2.9
	Surgery alone		1	2.9
	Surgery followed by chemotherapy		3	8.6

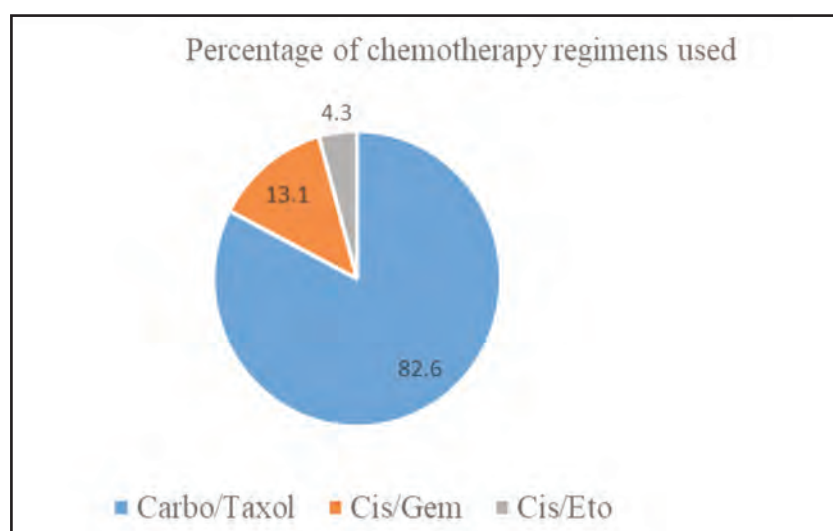


Fig. 1: Percentage of chemotherapy regimens used

metastases at less common sites (other sites) were associated with significantly shorter PFS. Patients with metastases at these sites had a median PFS of four months, compared to seven months for those without, with a p-value of 0.025. This difference, however, was not statistically significant for OS.

Nevertheless, the Kruskal-Wallis H non-parametric test showed no statistical differences between the groups in terms of cancer status at initial diagnosis, histology subtypes, and number of metastatic sites for both PFS and OS, as demonstrated in Table II.

Kaplan-Meier survival estimates for metastatic disease at other sites

As explained previously, metastatic sites were grouped based on the common sites of metastasis which were lung, liver, bone, nodal, and local recurrence. However, metastasis at the less common sites were separated as one group and there were four patients in this group. Out of these four patients, two had metastasis at adrenal glands, one patient had both

peritoneal and adrenal metastases, and another one patient had peritoneal metastasis. This group of patients showed significant effect statistically in PFS by Mann-Whitney U test, hence we further conducted Kaplan-Meier survival analysis.

The patients with metastatic disease showed median PFS of four months (95% CI: 0.61 to 7.39 months) while the patients without presence of metastatic disease at these sites showed PFS of six months (95% CI: 4.5 to 7.49 months). The Log-Rank (Mantel-Cox) test yielded a Chi-square statistic of 8.14 with a p-value of 0.004 indicating a statistically significant difference in survival times between the groups. This result indicates that cervical carcinoma with metastasis at less common sites such as peritoneal and adrenals had poorer outcomes. The Kaplan-Meier survival estimates was also conducted for overall survival. However, although median OS for patients with metastasis at other sites was only four months compared to 12 months for patients who did not have the metastasis, they were not statistically significant with a p-value of 0.062.

Patterns of management

Table IV demonstrates the descriptive analysis of management of the patients with metastatic/recurrent cervical carcinoma in Department of Clinical Oncology, UMMC. The most commonly employed treatment modality was palliative chemotherapy, administered to 68.6% of the patients, followed by radiation therapy, which was used in 57.1% of the patients. A small number of the patients had debulking surgeries. 17.1% of the patients were treated conservatively with best supportive care.

Almost half of the patients (45.7%) had combination of treatment modalities as their first line management, either chemotherapy followed by radiotherapy (RT), radiotherapy followed by chemotherapy, or surgery followed by chemotherapy. One patient had surgery alone as she passed away shortly after the surgery. Four patients had radiotherapy alone mainly due to patients' refusal for chemotherapy.

For patients who had chemotherapy, combination of carboplatin-paclitaxel (carbo/taxol) was the most commonly used regimen, followed by gemcitabine-cisplatin (cis/gem). 1 patient with neuroendocrine carcinoma had cisplatin-etoposide (cis/eto) regimen as illustrated in Figure 1.

DISCUSSION

This retrospective study aimed to evaluate the survival outcomes of the patients with metastatic/recurrent cervical carcinoma registered at the Department of Clinical Oncology, UMMC. In addition to that, the study aimed to analyse demographic and tumour characteristics that may influence the survival in this cohort of cancer patients as well as patterns of management practised.

This study reported that the median progression-free survival (PFS) for metastatic/recurrent cervical cancer was six months, while median overall survival (OS) was 12 months. These findings were consistent with previous studies, notably Bonomi et al., Moore et al. and Monk et al., where they reported PFS ranged from 3.9 to 6.9 months and median OS ranged from 9.9 to 12.87 months.⁵⁻⁷ Our study also showed that there was a moderate positive correlation between the PFS and OS. Patients who had longer PFS tended to have longer OS and vice versa. Although PFS has yet to be established as a validated surrogate endpoint for OS, a meta-analysis by Yarza et al. suggested that PFS may serve as a potential surrogate endpoint depending on treatment strategies.⁸ However, further prospective studies are required to confirm this association.

This study found that 37.2% of cervical cancer patients at this centre were diagnosed with metastatic/recurrent disease, either as de novo or recurrent cases. This incidence was significantly higher than both global reports (10–30%) and national data, where the MNCR reported only 21.7% of metastatic cervical cancer cases between 2017 and 2021.^{3,9} However, this study had included the cases of recurrent diseases either at distant sites or local recurrences that were not amenable to curative treatment, hence were treated as

per metastatic diseases. This had contributed to higher prevalence compared to national or global reports.

The demographic factors evaluated in this study were age, ethnicity, performance status by ECOG, and comorbidities. This study reported that the occurrence of metastatic/recurrent disease increased with increasing age, particularly after the age of 40 years old. This was consistent with the MNCR report, which also reported a marked increase in cervical cancer after the age of 40 years old.⁹ More than 50% of the patients were of Chinese ethnicity, which again reflected the national registry, which reported that Chinese origin has a higher lifetime risk of cervical cancer compared to Malay or Indian races. No statistically significant differences in patients' survival were observed across the groups stratified by performance status, and comorbidities.

Tumour characteristics evaluated in this study included cancer status at initial diagnosis, histological subtypes, and metastatic sites (both location and number of sites involved). The analysis found no statistically significant association between initial cancer status and patients' survival. However, local recurrence and nodal metastases were prevalent within these patients' cohort. These findings emphasised the importance of management in early-stage cervical cancer to reduce the risk of recurrence, hence survival.

Squamous cell carcinoma (SCC) was the most common histological subtype in this cohort 68.6%, followed by adenocarcinoma 28.6%. One patient was diagnosed with neuroendocrine carcinoma. These findings were consistent with global epidemiological trends.⁴ Although many studies reported that adenocarcinoma demonstrated poorer survival outcomes compared to the SCC subtype in the overall population of cervical cancer patients, comparisons in metastatic/recurrent settings were scarce.¹⁰ Nevertheless, the findings of the present study, which demonstrated no significant difference in survival outcomes between SCC and adenocarcinoma subtypes, were consistent with those of the NRG Oncology/Gynaecologic Oncology Group study led by Seamon et al., which reported comparable outcomes in patients with metastatic cervical carcinoma between the groups.¹¹

Human papillomavirus (HPV) infection is recognised as the primary risk factor in the epidemiology of cervical cancer.² However, HPV association was not studied in this survey, as it was not a standard practice for HPV reporting in our centre. Hence, the analysis may have led to misinterpretation.

The majority of patients in this cohort demonstrated local and nodal recurrence, emphasising the importance of timely and optimal management during the early stages of disease. However, among visceral metastases, lung was the most commonly affected site, followed by bone and liver involvement. This pattern was consistent with findings from a large population-based study by Zhou et al., which reported lung metastases in 37.9% of 1,347 patients.¹² Similarly, most patients in the current study presented with metastases confined to a single site.

Distant metastases at sites other than nodal regions, local recurrence, lung, bone, or liver were associated with significantly worse survival outcomes. This suggested that metastases to fewer common sites, such as the peritoneum and adrenal glands, may be associated with more aggressive diseases and poorer prognoses, although evidence was scarce due to their rarity. However, the number of metastatic sites did not have a significant impact on survival.

This study demonstrated a variety of management approaches for metastatic cervical carcinoma, including best supportive care, chemotherapy alone, chemotherapy followed by radical radiotherapy, chemotherapy followed by palliative radiotherapy, radical radiotherapy alone, palliative radiotherapy alone, radical radiotherapy followed by chemotherapy, palliative radiotherapy followed by chemotherapy, surgery alone, and surgery followed by radiotherapy.

Although the optimal management of metastatic/recurrent cervical carcinoma remained debated, many studies and clinical guidelines recommended initiating systemic treatment.⁴ This was consistent with our findings, where chemotherapy alone or in combination with other modalities were the most frequently used treatment modalities, together accounting for 68.6% of the patients in this cohort.

Historically, single-agent intravenous cisplatin was the most commonly used chemotherapy for metastatic cervical carcinoma. However, in this study, all patients who received chemotherapy were treated with doublet regimens. Carboplatin-paclitaxel was the most frequently administered combination, while cisplatin-gemcitabine and cisplatin-etoposide were used in a minority of cases. This practice was concordant with international guidelines, supported by landmark trials demonstrating improved survival outcomes with doublet regimens.⁶⁻⁷ Since 2015, Kitagawa and colleagues reported the non-inferiority of carboplatin-paclitaxel compared to cisplatin-paclitaxel, with the added benefit of better quality of life.¹³ Although bevacizumab and immunotherapy had been shown to improve outcomes in metastatic cervical cancer, none of the patients in this cohort received these agents, likely due to financial constraints, as bevacizumab and immunotherapy were not reimbursed by standard government funding in Malaysia.¹⁴⁻¹⁶

The main limitation of this study was its small sample size and retrospective nature. Hence, there were risks of inaccuracy in data reporting, which may affect the analysis. Although UMMC is one of the few cancer centres in Malaysia, due to the sudden Coronavirus-19 pandemic that hit the country in 2019-2021, accessibility was restricted. The management of the patients was also affected; as national healthcare efforts were directed towards addressing the pandemic. Besides that, the accessibility and affordability of the newer agents, particularly bevacizumab, had also improved over the past few years due to the availability of a generic version of bevacizumab, which may demonstrate better results and outcomes. Therefore, future researches should include multicentre studies, as they may provide more robust data and allow for a more comprehensive evaluation of treatment effects and their tolerability in relation to survival outcomes.

In addition, this study only looked at the first-line systemic therapies. Therefore, further studies are needed to evaluate the effects of subsequent therapies in survival of metastatic/recurrent cervical cancer.

CONCLUSION

The median progression-free survival of six months and median overall survival of 12 months were consistent with global survival statistics, hence suggesting that local treatment practices were comparable to the international standards.

The data also indicated that middle-aged women represented the most affected demographic, emphasising the need for targeted cancer screening, education, and prevention programmes to enhance awareness and promote early detection within this population. Additionally, this study demonstrated that the majority of metastatic/recurrent cervical cancer cases developed as a progression from early-stage disease. This emphasised the importance of optimal management during radical treatment, particularly ensuring timely initiation of therapy and access to oncological services.

The management of metastatic/recurrent cervical cancer in Malaysia was consistent with international recommendations and studies. However, none of the patients in this cohort had received newer therapeutic agents such as bevacizumab or pembrolizumab, which may have prolonged their survival outcomes. Therefore, efforts and support to enhance accessibility to these newer therapies should be improved at the national level for better outcomes.

REFERENCES

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024; 74(3): 229-63.
2. Zhang S, Xu H, Zhang L, Qiao Y. Cervical cancer: epidemiology, risk factors and screening. *Chin J Cancer Res*. 2020; 32(6): 720-8.
3. Li H, Wu X, Cheng X. Advances in diagnosis and treatment of metastatic cervical cancer. *J Gynecol Oncol* 2016; 27(4): e43.
4. Marth C, Landoni F, Mahner S, McCormack M, Gonzalez-Martin A, Colombo N, et al. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2017; 28(Suppl 4): iv72-83.
5. Bonomi P, Blessing JA, Stehman FB, DiSaia PJ, Walton L, Major FJ, et al. Randomized trial of three cisplatin dose schedules in squamous-cell carcinoma of the cervix: a Gynecologic Oncology Group study. *J Clin Oncol* 1985; 3(8): 1079-85.
6. Moore DH, Blessing JA, McQuellon RP, Thaler HT, Cella D, Benda J, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. *J Clin Oncol* 2004; 22(15): 3113-19.
7. Monk BJ, Sill MW, McMeekin S, Cohn DE, Ramondetta LM, Boardman CH, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma. *J Clin Oncol* 2009; 27(28): 4649-55.
8. Yarza R, Kountouri M, Guedes H, O'Gorman C, Estrada-Lorenzo JM, Coens C, et al. Progression-free survival as a potential surrogate end point for overall survival in advanced cervical carcinoma. *Int J Gynecol Cancer* 2024; 35(2): 100012.

9. Institut Kanser Negara. The Malaysia National Cancer Registry Report 2017-2021. Putrajaya: National Cancer Registry Department, Ministry of Health Malaysia; 2021.
10. Zhang Y, Shu P, Wang X, Ouyang G, Zhou J, Zhao Y, et al. Comparison of survival between different histological subtypes in cervical cancer patients: a retrospective and propensity score-matched analysis. *J Cancer* 2024; 15(19): 6326-35.
11. Seamon LG, Java J, Monk BJ, Leath CA 3rd, Schmeler KM, Eifel PJ, et al. Impact of tumour histology on survival in advanced cervical carcinoma: an NRG Oncology/Gynaecologic Oncology Group study. *Br J Cancer* 2018; 118(2): 162-70.
12. Zhou S, Peng F. Patterns of metastases in cervical cancer: a population-based study. *Int J Clin Exp Pathol* 2020; 13(7): 1615-23.
13. Kitagawa R, Katsumata N, Shibata T, Kamura T, Kasamatsu T, Nakanishi T, et al. Paclitaxel plus carboplatin versus paclitaxel plus cisplatin in metastatic or recurrent cervical cancer: the open-label randomized phase III trial JCOG0505. *J Clin Oncol* 2015; 33(19): 2129-35.
14. Tewari KS, Sill MW, Long HJ, Penson RT, Huang H, Ramondetta LM, et al. Improved survival with bevacizumab in advanced cervical cancer. *N Engl J Med* 2014; 370(8): 734-43.
15. Tanigawa T, Takeshima N, Ishikawa H, Nishio S, Usami T, Yamawaki T, et al. Paclitaxel-carboplatin and bevacizumab combination with maintenance bevacizumab therapy for metastatic, recurrent, and persistent uterine cervical cancer: an open-label multicenter phase II trial (JGOG1079). *Gynecol Oncol* 2022; 165(3): 413-19.
16. Colombo N, Dubot C, Lorusso D, Caceres MV, Hasegawa K, Shapira-Frommer R, et al. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. *N Engl J Med* 2021; 385(20): 1856-67.