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The new FIGO 2023 staging reclassification of patients with FIGO 2009 Stage IVB endometrial cancer correlates to progression-free and overall survival outcomes

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ABSTRACT

Objective: This study aims to determine the oncological outcomes of Stage IVB (FIGO 2009) Endometrial cancer patients and its comparison with the new (FIGO 2023) staging.
Methods: A Retrospective analysis was conducted between May 30, 2011, and December 30, 2020 on all patients with stage IVB (FIGO 2009 Staging) endometrial cancer. Overall survival (OS) was the primary outcome. Progression-Free Survival (PFS) and comparison with new staging FIGO 2023 were the secondary outcomes. Kaplan-Meier curves and log-rank tests were used to compare the average OS time and PFS between the groups.
Results: Fifty-one patients with Stage IVB endometrial cancer (2009 FIGO Staging) were included. Median age was 68 years. Serous histology was found in 24 (47.1 %) patients. After a median follow-up period of 24 months, median OS was 36 months and median PFS was 15 months. FIGO 2023 staging criteria reclassified the stages of 23 patients (45 %). Patients were restaged into Stage IIIB2 (9.8 %), IVA (5.8 %), IVB (55 %) and IVC (29.4 %). Median OS and PFS were not reached for stages IIIB and IVA, while the median OS and median PFS for stage IVB were 36 months and 18 months, respectively. However, patients with stage IVC had lower median OS and PFS of 10 months and 4 months, respectively.
Conclusion: The clinical outcomes of patients with Stage IVB are varied depending mainly on the disease distribution. Patients with abdominal or pelvic disease had better survival outcomes and therefore, needed a different categorisation. Thus, FIGO 2023 Staging considers this varied disease distribution and appears to be a better prognostic indicator for this group.

1. Introduction

Endometrial cancer (EC) is the sixth most common malignancy in women worldwide and the third most common gynaecological malignancy in India, with a reported incidence of 17,420 new cases in 2022 (Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global Cancer Statistics, 2022). Although EC is present at an early stage in 90 % of the cases, about 10 % of newly diagnosed patients present at an advanced stage having a five-year survival rate ranging from 0-20 % (Agarwal et al., 2023; Colombo et al., 2013). Primary Debulking Surgery (PDS) is considered a standard treatment for advanced endometrial cancer if optimal cytoreduction is feasible. However, in patients where complete cytoreduction is not deemed possible, Neoadjuvant Chemotherapy (NACT) followed by Interval Debulking Surgery (IDS) may be administered (Berek et al., 2023 Aug). Nevertheless, there are no definitive established criteria for the management of Stage IV endometrial cancers due to their rarity and heterogeneous presentation, and they differ in different institutions.

FIGO 2009 staging defines Stage IVB as a disease involving pelvic peritoneum, intra-abdominal spread, or extra-abdominal metastasis. Stage IVB has been further elaborated and modified by FIGO 2023 staging. It has redefined Stage IVB as a disease limited to the abdomen and included extra-abdominal metastasis in Stage IVC. Pelvic peritoneal disease is classified as stage IIIB2 (Abu-Rustum et al., 2023 Feb).

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Due to the rare incidence of EC patients presenting with Stage IVB, literature on their prognosis is scant. In addition, the management strategies of these patients are not uniform overall. The new staging system must still be clinically applied at different oncological centres. With this background, our study aims to investigate the outcomes of Stage IVB (2009 staging) patients and to evaluate the stage-wise outcomes after applying the FIGO 2023 staging criteria. We hypothesised that reclassifying patients with stage IVB endometrial cancer from the FIGO 2009 staging to the new FIGO 2023 staging would be better correlated with progression-free and overall survival outcomes.

2. Materials and methods

A retrospective analysis of 51 patients with Stage IVB (FIGO 2009) endometrial cancer was conducted over ten years, from May 30, 2011, to December 30, 2020, after the approval of our Institutional Review Board (IRB no. IEC-AIMS-2024-GYNAEC ONCO-104).

All cases of stage IVB (according to the FIGO 2009 staging system) endometrial cancers that were diagnosed based on clinical findings, radiological imaging, or histopathology and were managed in our hospital from 2011 to 2020, regardless of the treatment given and histology were included in the study. Patients with less than three months of follow-up were excluded. The primary objective was to determine the 3-year median Overall Survival (OS) and 3-year median Progression-Free Survival (PFS) of patients with Stage IVB Endometrial Cancer. Secondary Objectives were to Compare the OS and PFS of patients with Stage IVB endometrial cancer between the 2009 FIGO Staging system and the 2023 FIGO Staging system, to evaluate the treatment patterns received by these patients and their outcomes based on the different treatment patterns and to assess the significant risk factors associated with OS and PFS.

2.1. Institutional Protocol

The primary treatment plan was determined based on the patient's ECOG status, disease extent, and likelihood of achieving optimal cytoreduction. Patients who had extensive abdominal or pelvic peritoneal disease necessitating complex procedures that they did not consent to, as well as those with multiple comorbidities preventing complex procedures, poor ECOG status (Colombo et al., 2013; Berek et al., 2023 Aug), doubtful potential for achieving optimal cytoreduction, and those with distant metastasis, received upfront chemotherapy. After receiving 3–4 cycles of neoadjuvant chemotherapy (NACT), patients underwent reassessment to determine the feasibility of optimal cytoreduction using imaging such as contrast-enhanced CT Chest/abdomen/pelvis or Whole Body PETCT. Those who responded partially to chemotherapy underwent IDS, while poor responders were only given chemotherapy. IDS was performed using either an open approach or a minimally invasive surgery (MIS) approach. MIS was performed using a robotic approach if the disease was confined to the pelvic peritoneum or only involved the omentum in the upper abdomen. Patients who underwent primary debulking surgery (PDS) or IDS after NACT received additional adjuvant treatment in the form of chemotherapy, with or without radiation. The decision on whether to combine radiation with chemotherapy was made during a Multidisciplinary Tumour Board (MDTB) meeting and was typically reserved for cases of extensive local disease. An immunohistochemistry (IHC) panel was performed on the preoperative endometrial biopsy, including ER, PR, and p53 staining. LVSI was not documented in the preoperative biopsy reports but was only available in the postoperative histopathology reports.

The following parameters were collected:

2.2. Clinicopathological characteristics and follow up

Clinical features, including the patient's age, ECOG performance status, clinical presentation and pattern of disease spread through imaging, were collected. The treatment pattern and histopathological parameters such as histology type, lymphovascular space invasion (LVSI), and staging were noted. Data on the type of Neoadjuvant Chemotherapy administered, number of cycles, response rate, and interval duration of surgery after chemotherapy were also collected. Adjuvant treatment was categorised into a single modality (chemotherapy or radiotherapy) or combined modality (chemotherapy + radiotherapy). Patients were followed up for recurrence or progression till September 30, 2023. The number of patients who progressed or recurred, the site of progression or recurrence and the treatment modality administered were recorded.

2.3. Reclassification using FIGO 2023 Staging

According to the new 2023 FIGO staging criteria, patients previously diagnosed with IVB endometrial cancer (based on the 2009 FIGO criteria) may now be recategorised into stages IIIB, IIIC, IVB, or IVC. Under the 2023 FIGO staging criteria, patients with pelvic peritoneal disease were downstaged to IIIB2. If they had pelvic peritoneal disease and enlarged nodes, they were downstaged to stage IIIC. Stage IVB is defined as abdominal peritoneal metastasis or intraperitoneal carcinomatosis beyond the pelvis. Stage IVC is defined as distant metastasis that includes the inguinal lymph nodes, lungs, liver, and bone. We reclassified our cohort according to the new 2023 FIGO staging criteria based on surgical pathology at the time of cytoreduction. Pre-operative imaging was also used for accurate staging, and those with distant metastases on imaging were classified as IVC, regardless of the availability of tissue biopsy.

2.4. Statistical Analysis

Statistical analyses were performed using the IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, IL, USA). The results are presented as mean ± SD for all continuous variables and as frequency (percentage) for categorical variables. PFS was defined as the time between the date of surgery and the documented recurrence date. OS was defined as the time between the date of diagnosis and date of death from any cause. Kaplan-Meier curves and log-rank tests were used to compare the average OS time and PFS between the groups. Statistical significance was set at $p < 0.05$. All statistical significance tests were two-tailed.

3. Results

3.1. Demographic Profile

Clinicopathological characteristics and treatment details received by the patients are shown in Table 1.

Fifty-one patients with Stage IVB EC (2009 FIGO Staging) were included in the study. The median patient age was 68 years (range: 61–70 years). The majority of patients (n = 41, 80 %) presented with abdominal symptoms, including abdominal pain, discomfort, abdominal distension, and gynaecological complaints, including postmenopausal bleeding, abnormal uterine bleeding, or discharge per Vaginum. One patient was diagnosed during an evaluation for DVT, and the other was diagnosed incidentally during a routine checkup. One patient had a history of colon cancer and was diagnosed with Lynch syndrome, while another patient had a history of breast cancer. Most patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 1 (n = 40, 78.4 %), while 11 (21.7 %) patients had an ECOG status of 2–3.

3.2. Work-up and treatment given

The patients were evaluated using different imaging modalities, such as CE-MRI (n = 22, 43 %), CECT (n = 20, 39.2 %) and PET-CT (n = 9, 17.6 %). Twenty-two (43 %) patients had disease confined to both the pelvis and abdomen, the pelvis-limited disease was present in 11

Table 1
Clinico-pathologic Characterisitics of patients with Stage IVB Endometrial Cancer.

Parameters	Subcategory	N (51)	%
AGE (years)	<40	1	2
	41–50	12	23.5
	51–60	18	35.3
	61–70	20	39.2
ECOG	1	40	78.4
	2	9	17.7
	3	2	4
DISEASE DISTRIBUTION	Isolated Pelvic confined	11	21.5
	Isolated Abdominal	4	7.8
	Isolated Distant metastasis	1	2
	Abdomen and Pelvis Confined	22	43.1
	Pelvis, Abdominal and distant metastasis	13	25.4
HISTOLOGY TYPE	Endometroid	16	31.3
	Serous	24	47
	Other Histologies	11	21.5
p53 MUTATION	Wild Type	12	23.5
	Mutated	27	53
	Not Available	12	23.5
Her2neu	Negative	15	92.1
	Positive	4	7.8
LVSI	Negative	3	5.8
	Positive	22	43.11
	Not Assessed	26	51
TYPE	Endometroid	16	31.3
	Serous	24	47
	Other Histologies	11	21.5
UPFRONT TREATMENT	PDS	21	41
	Chemotherapy only	21	41
	NACT + IDS	9	17.6
DEGREE OF CYTOREDUCTION	Optimal	27	90
	Suboptimal	3	10
MODE OF SURGERY FOR PDS/IDS	Open	20	66.6
	MIS	10	33.3
NACT RESPONSE	Partial	9	30
	Poor	21	70
ADJUVANT TREATMENT	Chemotherapy only	9	32
	Chemotherapy + Radiotherapy	19	68
PROGRESSION/ RECURRENCES	None	13	25.5
	Yes	38	74.5

patients (21.5 %), distant metastases were present in 13 patients (27.5 %), and isolated distant metastasis was found in 1 patient (2 %). Distant metastases were found in the supraclavicular lymph nodes (n = 4), liver (n = 4), lungs (n = 6), bone (n = 6), and mediastinal lymph nodes (n = 3). The primary treatment modality was PDS (n = 21, 41.2 %), only Chemotherapy (n = 21, 41.2 %) and NACT followed by IDS (n = 9, 17.6 %). The surgeries were done using minimally invasive or an open route in 10 patients (33.3 %) and 20 patients (66.6 %). MIS was performed on patients with disease distribution as follows: omentum (n = 4), pouch of Douglas peritoneum (n = 4), bladder peritoneum (n = 2), and sigmoid mesocolon (n = 3). Overall, optimal cytoreduction was achieved in 90 % (n = 27) of patients.

3.3. Histo-Pathological Characteristics

Serous histology was found in most patients (n = 24, 47 %). Substantial LVSI was seen in 22 (43.1 %) patients. IHC tests performed included ER, PR, and p53. Patients with ER, PR, and p53 were 31 (60 %), 13 (25.4 %), and 27 (53 %) respectively. Her2 testing was conducted in cases where the disease had progressed. It was performed on 14 patients, of whom 4 tested positive on IHC. Three patients had p53 mutations, while one patient had wild-type p53. LVSI information was accessible for all 21 patients who had PDS and for 4 out of 9 patients who had IDS. However, medical records did not contain LVSI information for 5 IDS patients. LVSI positivity was identified in 22 out of these 25 patients.

3.4. Adjuvant treatment

Twenty-eight out of thirty patients (93.3 %) underwent PDS or IDS were given adjuvant treatment. Two patients received only palliative therapy in the form of symptomatic care, as they were not fit for taking adjuvant therapy due to postoperative complications (infected wound and dyselectrolytemia). During adjuvant treatment, three patients progressed on treatment and expired. The most commonly used chemotherapy regimen was carboplatin plus paclitaxel. Pelvic Radiation was added in cases of pelvic disease involvement after the MDTB meeting. Most patients received combined chemotherapy (3–4 cycles) + Pelvic Radiation (n = 19, 67.8 %).

3.5. Reclassification by 2023 FIGO staging criteria

Restaging was performed based on the final histopathologic report for those who underwent PDS, while it was done using imaging for those who did not have upfront surgery. After applying the 2023 FIGO staging criteria, 23 patients (45 %) underwent a change in stage. Patients were reclassified into Stage IIIB2 (n = 5, 9.8 %), IVA (n = 3, 5.8 %), IVB (n = 28, 55 %) and IVC (n = 15, 29.4 %). The redistribution of clinicopathological parameters is elicited in Table 2. All patients diagnosed with new Stage IIIB disease had undergone primary cytoreduction. Among the new stage IVB patients, 14 patients (50 %) underwent PDS. The remaining 14 patients received upfront chemotherapy. Of these, 8 patients (28.5 %) underwent IDS, and 6 patients (21.4 %) received only chemotherapy. The majority of stage IVC patients were treated with only chemotherapy (n = 13, 86.6 %). IDS was performed on one patient with resolved supraclavicular lymph nodes after NACT. Only one patient with stage IVC disease involving inguinal lymph nodes underwent PDS and achieved optimal cytoreduction.

3.6. Survival Outcomes

The median follow-up period was 24 months (3–120 months). Patients lost to follow-up (n = 7) were censored at their last follow-up date. Patients who were alive were censored on 30 December 2023. Out of 51 patients, 35 (68.6 %) experienced death. Among the deceased, 31 patients died due to disease progression or recurrences, while 4 died due to other causes. Disease progression or recurrences were observed in a total of 38 (74.5 %) patients, out of which 31 passed away and 7 patients were still alive. The 3-year median OS was 36 months (95 % CI 23.5–48.4 months). The 3-year median PFS was 15 months (95 % CI 8.2–21.7 months). The most common site for progression/recurrences was the pelvis (n = 26, 54 %), followed by the abdomen (n = 15;29.4 %) and distant metastasis (n = 10; 19.6 %).

NACT with IDS led to significant improvement ($p = 0.04$) in PFS compared with PDS, with PFS durations of 32 and 16 months, respectively. However, the OS was similar between the NACT with IDS and PDS groups, with median OS durations of 47 and 49 months, respectively. In contrast, patients who received only chemotherapy as upfront treatment exhibited poor outcomes, with median OS and PFS durations of 10 months and 3 months, respectively. Poor ECOG status and single adjuvant treatment modality were associated significantly with worse OS ($p < 0.05$). Poor ECOG status and distant metastasis were significantly associated with worse PFS ($p < 0.05$). Details of clinical and pathological factors associated with survival are shown in Table 3.

3.7. Survival outcomes after applying FIGO 2023 staging:

The 3-year median OS could not be reached for stages IIIB and IVA, whereas the 3-year median OS for Stage IVB was 36 months (95 % CI 21.6–50.3 months) and for Stage IVC was 10 months (95 % CI 3.6–16.3 months) (Fig. 1). The 3-year median PFS could not be reached for stages IIIB and IVA, while it was 18 months (95 % CI 7.8–28.1 months) for Stage IVB and four months (1.6–6.3 months) for Stage IVC (Fig. 2).

Table 2
Redistribution of Clinico-Pathologic Characteristics According to New FIGO 2023 Staging.

PARAMETERS	SUBCATEGORY	FIGO 2009 STAGING n = 51 (%)	FIGO 2023 STAGING			
			IIIB (n = 5)	IVA (n = 3)	IVB (n = 28)	IVC (n = 15)
AGE (years)	<40	1 (2 %)	0	0	0	1 (6.6 %)
	41–50	12 (23.5 %)	2 (40 %)	1 (33.3 %)	7 (25 %)	2 (13.3 %)
	51–60	18 (35.3 %)	2 (40 %)	0	10 (35.7 %)	6 (40 %)
	61–70	20 (39.2 %)	1 (20 %)	2 (66.6 %)	11 (39.2 %)	6 (40 %)
ECOG	1	40 (78.4 %)	4 (80 %)	2 (66.6 %)	23 (82.1 %)	11 (73.3 %)
	2	9 (17.6 %)	0	1 (33.3 %)	5 (17.9 %)	3 (20 %)
	3	2 (4 %)	1 (20 %)	0	0	1 (6.6 %)
DISEASE DISTRIBUTION	Pelvic confined	11 (21.5 %)	5 (100 %)	3 (100 %)	2 (7.1 %)	1 (6.6 %)
	Isolated Abdominal	4 (7.8 %)	0	0	2 (7.1 %)	2 (13.3 %)
	Isolated Distant metastasis	1 (2 %)	0	0	0	1 (6.6 %)
	Pelvic and abdominal	22 (43.1 %)	0	0	22 (78.5 %)	0
	Pelvic, abdominal and metastatic	13 (25.4 %)	0	0	2 (7.1 %)	11 (73.3 %)
p53 MUTATION	Wild Type	12 (23.5 %)	1 (20 %)	0	7 (25 %)	4 (26.6 %)
	Mutated	27 (53 %)	2 (40 %)	0	17 (60.7 %)	8 (53.3 %)
	Not Available	12 (23.5 %)	2 (40 %)	3 (100 %(	4 (14.2 %)	3 (30 %)
HISTOLOGICAL TYPE	Endometroid	16 (31.5 %)	3 (60 %)	1 (33.3 %)	9 (32.1 %)	3 (30 %)
	Serous	24 (47 %)	2 (40 %)	1 (33.3 %)	17 (60.7 %)	4 (26.6 %)
	Other Histologies	11 (21.5 %)	0	1 (33.3 %)	2 (7.1 %)	8 (53.3 %)
UPFRONT TREATMENT GIVEN	PDS	21 (41 %)	5 (100 %)	1 (33.3 %)	14 (50 %)	1 (6.6 %)
	Chemotherapy only	21 (41 %)	0	2 (66.6 %)	6 (21.4 %)	13 (86.6 %)
	NACT + IDS	9 (17.5 %)	0	0	8 (28.5 %)	1 (6.6 %)
MODE OF SURGERY (n = 30)	Open	20 (66.6 %)	3 (60 %)	1 (33.3 %)	14 (50 %)	2 (13.3 %)
	Minimally Invasive	10 (33.3 %)	2 (40 %)	0	8 (28.5 %)	0
ADJUVANT TREATMENT (n = 28)	Chemotherapy + Radiotherapy	19 (68 %)	3 (60 %)	1 (100 %)	15 (54.5 %)	0
	Only Chemotherapy	9 (32 %)	1 (40 %)	0	8 (36.3 %)	0

Table 3
Oncological Outcomes of different Clinico-Pathological Parameters in patients with Stage IVB Endonetrial Cancer.

PARAMETERS	SUBCATEGORY	OVERALL SURVIVAL	P VALUE	PROGRESSION-FREE SURVIVAL	P VALUE
AGE (years)	<40	Not Reached	0.07	Median Not Reached	0.07
	41–50	49 months (44.2–53.7)		32 months (4.5–59.4)	
	51–60	24 months (13.6–34.4)		16 months (8.9–23)	
	61–70	11 months (4.7–17.3)		10 months (3.3—16.6)	
ECOG	1	47 months (24–64.5)	0.005	19 months (13–25)	0.04
	2	6 months (0–13.7)		3 months (0–9.8)	
	3	0 %		0 %	
DISEASE DISTRIBUTION	Pelvis confined	Median not Reached	0.12	16 months (0–68.2)	0.05
	Isolated Abdomen	21 months (0–60)		19 months (2.3–35.6)	
	Pelvis and Abdomen	26 months (0–57)		15 months (7.5–22.4)	
	Pelvis or Abdomen with distant metastases	11 months (0–37)		11 months (0—24.1)	
HISTOLOGICAL TYPE	Serous	39 months (14.7–63.2)	0.79	19 months (5.6—32.3)	0.11
	Other Histologies	10 months (5.1–14.8)		4 months (0–12.6)	
	Endometroid	38 months (13.5–62.4)		15 months (8.6–21.3)	
UPFRONT TREATMENT GIVEN	Chemotherapy only	10 months (0–26.4)	0.60	3 months (1.31–4.68)	0.04
	NACT + IDS	47 months (19.6–74.3)		32 months (6.23—57.7)	
	PDS	49 months (1.4–96.3)		16 months (9.4–22.5)	
MODE OF SURGERY	Open	29 % 48 months (6.5–89.4 months)	0.60	20 % 18 months (1.9–34 months)	0.12
	Minimally Invasive	46.7 % Median not reached		38 % Median Not Reached	
MULTIMODALITY ADJUVANT TREATMENT	Chemotherapy + Radiotherapy	48 months (44.5–51.4)	**0.03**	31 months (11.3–50.6)	0.95
	Only Chemotherapy	11 months (0–35.2)		25 months (4.1–45.8)	

Survival outcomes and comparison with the new staging are given in Table 4.

4. Discussion

Data regarding the outcomes of patients with stage IVB are scarce because of their infrequent incidence. Pelvic peritoneal disease, abdominal disease, or distant metastases are combined under Stage IVB as per the 2009 FIGO staging despite being prognostically different. With the introduction of the FIGO 2023 staging system, this stage has been redefined, prompting analysis of the differences in oncological outcomes between the old and new staging systems. The present study reports a real-world cohort of patients with stage IVB disease (2009 FIGO staging) with a 3-year median OS of 36 (95 % CI 23.5–48.4)

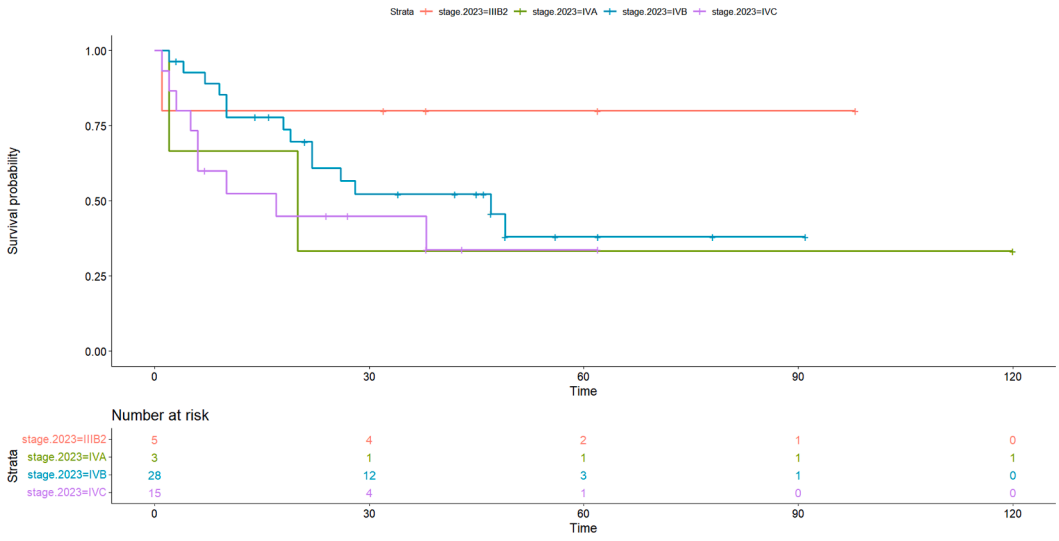

Fig. 1. Kaplan-Meier graph depicting median 3-year overall survival of patients classified according to FIGO 2023 Staging.

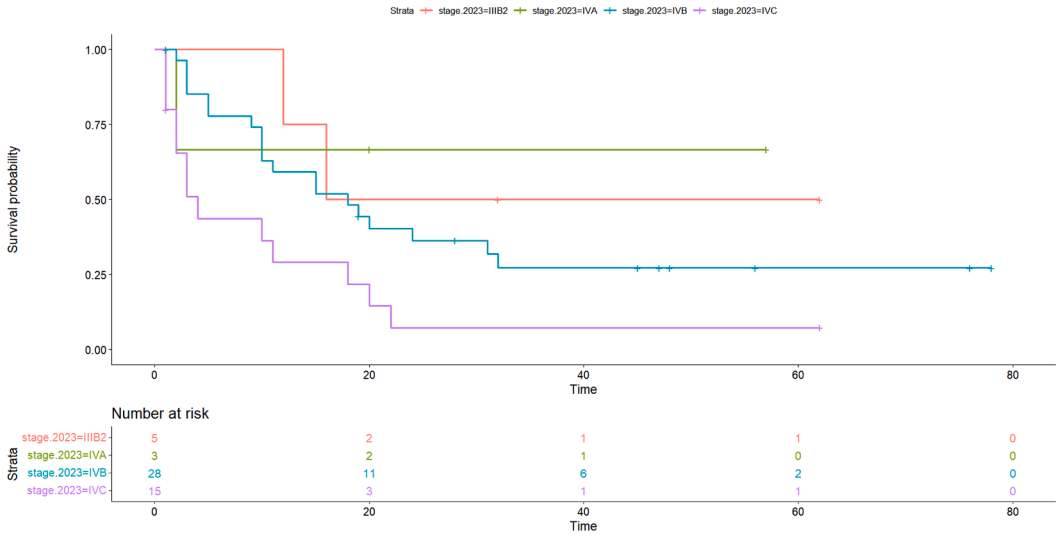

Fig. 2. Kaplan-Meier graph depicting median 3-year progression-free survival of patients classified according to FIGO 2023 Staging.

Table 4
Reclassification of Stage IVB Endometrial Cancer according to FIGO 2023 Staging and Comparison of their Oncological Outcomes.

	SUB-CATEGORY	IIIB	IVA	IVB	IVC
FIGO 2009 STAGING	**Number**	Not Included	Not Included	51	NA
	Overall Survival			36 months (23.5–48.4 months)	
	Progression-Free Survival			15 months (8.2–21.7 months)	
FIGO 2023 STAGING	**Number**	5 (9.8 %)	3 (5.8 %)	28 (55 %)	15 (29.4 %)
	Overall Survival (Median)	Median not Reached	Median not reached	36 months (21.6–50.3 months)	10 months (3.6–16.3 months)
	Progression-Free Survival (Median)	Median not Reached	Median not reached	18 months (7.8–28.1 months)	4 months (1.6–6.3 months)

months and 3-year median PFS of 15 (95 % CI 8.2–21.7) months. The OS reported in a multicenter retrospective study conducted by Eto et al. involving 426 patients was 14 months (Eto et al., 2012 Nov). Other studies have demonstrated OS between 10–38 months (Haight et al., 2023 Aug; Bristow et al., 2000 Aug; Goff et al., 1994 Feb; Numazaki et al., 2009 Aug) and PFS of eight months (Haight et al., 2023 Aug). The current study also reported similar OS and PFS.

Following the reclassification of the cohort according to FIGO 2023 staging criteria, 23 patients (45 %) underwent a change in stage. It has led to a redefinition of survival outcomes for these patients. For patients classified as Stage IIIB according to the new FIGO 2023 staging system, the median OS and PFS could not be determined, indicating potentially prolonged survival compared with the previous staging system where the median OS of the entire IVB cohort was 36 months and the median PFS was 15 months. This highlights the importance of distinguishing between patients with restricted pelvic peritoneal disease previously staged as IVB and those with distant metastasis. Patients with peritoneal deposits exhibited better outcomes than those with distant metastases. This evidence is corroborated by a recent study, A Surveillance, Epidemiology, and End Results Database study that reviewed more than 900

patients with FIGO 2009 stage IVB disease. It has shown a better prognosis in patients with peritoneal disease than in those with an organ-specific disease spread, thus eliciting the role of metastatic sites in prognostication (Li et al., 2020 Oct).

Treatment decisions for advanced endometrial cancer have historically been challenging owing to limited published literature. Despite PDS being the standard treatment for these patients, NACT has also shown promising outcomes when used as the initial approach in advanced settings (Eto et al., 2012 Nov; Vandenput et al., 2009 Jul; De Lange et al., 2019 Apr 1). These findings highlight the importance of individualised therapeutic strategies based on patient-specific factors and disease characteristics. Haight et al. demonstrated worse PFS with NACT, whereas OS rates were similar. However, NACT was significantly associated with higher disease stages when these patients were restaged according to the new staging system (Haight et al., 2023 Aug). In the present study, NACT with IDS significantly improved PFS compared with PDS alone (32 vs 16 months). However, the median OS was similar (47 vs 49 months). In contrast, patients who received only chemotherapy as upfront treatment exhibited poor outcomes (median OS: 10 months and median PFS: 3 months). Based on these results, upfront PDS with curative intent should be considered for patients with disease confined to the pelvis or abdomen, especially for those previously treated with palliative intent under the assumption of Stage IVB disease. This highlights the importance of re-evaluating treatment strategies based on updated staging criteria to improve patient outcomes. The possibility of performing minimally invasive surgeries in some patients with Stage IIIB and IVB disease, coupled with good survival outcomes compared with open surgeries, is noteworthy (OS: 46.7 % versus 29 %; PFS: 38 % versus 20 %). Most patients had optimal cytoreduction, so sub-optimal resection was not significantly associated with the stage.

There is always controversy on the administration of adjuvant therapy post-surgery or NACT + IDS. Owing to their heterogeneous presentation, no fixed evidence-based protocols concerning the best adjuvant treatment modality exist. Nevertheless, some studies have demonstrated the benefits of combined chemotherapy and radiotherapy over a single modality (Alvarezsecord et al., 2007 Nov; Kim et al., 2024 Mar; Tai et al., 2019 Jul 18). However, few studies have shown no difference in survival between combined or single adjuvant treatment modalities (Haight et al., 2023 Aug). The present study showed a significant improvement in overall survival for those who received combined chemotherapy (3–4 cycles) + Pelvic Radiation compared to patients who received only chemotherapy.

To our knowledge, this is the first Indian study to provide detailed management of Stage IVB disease and reclassify these patients according to the new FIGO 2023 staging system. This study also showed the outcomes of different treatment modalities and adjuvant treatments. The importance of segregating patients with pelvic or abdomen-confined diseases from extra-abdominal metastasis was also highlighted. This study had limitations due to its small cohort size, as advanced-stage endometrial cancer patients are rare. There was a lack of consistency in the imaging techniques used, and only a minority of patients underwent PET CT scans, potentially resulting in missed distant metastases. Moreover, distinguishing between Stage IIIC and Stage IIIB was not feasible because nodal staging was not conducted for advanced disease. Unfortunately, we couldn't perform a multivariate analysis for certain significant factors affecting survival outcomes because some categories required a larger sample size to ensure the study's validity. Therefore, conducting a multivariate analysis with a limited sample size would have yielded less meaningful results.

5. Conclusion

Thus, the present study demonstrated the clinical outcomes of IVB (FIGO 2009 staging) and the relevance of the FIGO 2023 staging system. This highlights the significance of changes in staging between the two systems, particularly in identifying patients with pelvis-confined disease who have a favourable prognosis compared to those with distant metastasis, which typically indicates poorer outcomes. In addition, options of NACT + IDS can be considered in patients whose optimal resection chances are less, as no difference in overall survival has been shown compared to patients with PDS. The new staging system offers advantages in defining the primary management plan more effectively, efficiently, and uniformly than the older system. Specifically, pelvic or abdominal peritoneum-confined disease may be suitable for primary cytoreduction, whereas cases with distant metastasis could be candidates for neoadjuvant chemotherapy. This streamlined approach enhances treatment decision-making and optimises therapeutic strategies tailored to patients' disease characteristics. Combining radiotherapy with chemotherapy for adjuvant therapy may lead to improved outcomes. However, since this is a single-centre study, it may be beneficial to conduct a multicenter study to emphasise better the impact of the new staging in advanced endometrial cancer cases.

Authors Contributions:

All authors contributed to the study's conception and design.

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CRediT authorship contribution statement

Monal Garg: Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Priya Bhati:** Writing – review & editing, Writing – original draft, Visualization, Validation, Conceptualization. **Pranidha Shree CA:** Writing – original draft, Formal analysis, Data curation. **Wesley M. Jose:** Writing – review & editing, Visualization, Validation, Supervision. **Sheejamol V.S.:** Methodology, Investigation, Formal analysis, Data curation. **Keechilat Pavithran:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Investigation.

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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