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Isolated vaginal recurrence in women with stage I endometrial cancer

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HIGHLIGHTS

- Isolated vaginal recurrences in stage I endometrial carcinoma were found in 2% of all patients with or without treatment.
- One percent of patients with treatment plans involving vaginal brachytherapy had an isolated vaginal recurrence.
- The most common location for isolated vaginal recurrences within the vagina was at the apex.
- Isolated vaginal recurrences were clinically detected sooner than extravaginal recurrences.
- Minimally invasive surgical approach did not affect recurrence rates.

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ABSTRACT

Objective. To compare clinical and pathologic characteristics of women with surgical stage I endometrial carcinoma by location of first recurrence and describe characteristics of isolated vaginal recurrence.

Methods. Patients with 2009 International Federation of Obstetrics and Gynecology (FIGO) stage I endometrial carcinoma treated at two large cancer centers from 1/1/2009–12/31/2017 were identified. Sarcoma histology was excluded. Recurrences were grouped into isolated vaginal or extravaginal. Isolated vaginal recurrences were localized by anatomic location within the vaginal vault. Clinical and pathologic variables were compared with chi-square analysis, and Kaplan-Meier curves with log-rank tests.

Results. Of 2815 women identified, 278 (10%) experienced a recurrence. Sixty-one patients (2%) had an isolated vaginal recurrence, including 42 (69%) at the vaginal apex; 217 (8%) had an extravaginal recurrence, including 18 with a vaginal component. Median time to recurrence was 11 months (range, 1–68) for isolated vaginal recurrence and 20 months (range, 1–98) for extravaginal recurrence ($P < .004$). Of 960 patients (34%) treated with adjuvant vaginal brachytherapy (VBT), 156 (16%) recurred; 19 (2%) had an isolated vaginal recurrence, including 16 (84%) at the vaginal apex. Three-year PFS rates for isolated vaginal recurrence were 97.6% (SE ± 0.4%) with minimally invasive surgery (MIS) versus 96.9% (SE ± 1.1%) with open ($P = .8$), and for extravaginal recurrence were 91.8% (SE ± 0.7%) with MIS versus 90.8% (SE ± 1.8%) with open ($P = .8$).

Conclusions. Isolated vaginal recurrences in stage I endometrial cancer are detected earlier than non-vaginal recurrences. Surgical approach does not appear to impact recurrence. Adjuvant VBT after primary surgery carries a 1%–2% risk of isolated vaginal apex recurrence.

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1. Introduction

In 2022, there were an estimated 66,200 new cases of endometrial cancer and 13,030 deaths from the disease [1]. Patients with uterine-confined disease are primarily treated with surgery including hysterectomy with or without bilateral salpingo-oophorectomy and regional lymph node assessment. Treatment for early-stage disease is guided by patient and pathologic risk factors including age, International Federation of Obstetrics and Gynecology (FIGO) grade, histology, depth of myometrial invasion, and presence of lymphovascular space invasion (LVSI) [2].

The use of radiation for recurrence control in early-stage endometrial cancer has been examined by the GOG-99 and Post-Operative Radiation Therapy in Endometrial Cancer (PORTEC-1) trials. These studies determined adjuvant external beam radiation therapy (EBRT) reduced the risk of recurrence in patients with high-intermediate risk (HIR) factors from 18%–26% to 5%–6% [3–5]. The improved locoregional control with EBRT, however, resulted in increased toxicity, including hematologic, genitourinary, gastrointestinal, and cutaneous adverse effects, as well as poorer long-term quality-of-life function within the gastrointestinal and genitourinary systems. Vaginal brachytherapy (VBT) emerged as a potential treatment based on findings from retrospective studies. PORTEC-2, a phase III noninferiority trial, subsequently determined VBT was effective in reducing locoregional recurrence, with an improved side-effect profile and similar oncologic survival compared to EBRT in patients with stage I and IIA endometrial carcinomas. The vaginal recurrence rate in this study was 1.8% in all patients who received VBT and 1.9% in those who received EBRT [6]. Other studies assessing VBT have also observed low rates of vaginal recurrence [7–11].

Despite excellent outcomes in patients with stage I endometrial carcinoma, there is a paucity of recent data describing and assessing recurrence patterns of this disease. The purpose of this study is to report the recurrence pattern for stage I endometrial carcinoma and to assess the clinicopathologic characteristics of isolated vaginal recurrence.

2. Methods

This study was approved through a joint Institutional Review Board (IRB) submission at Memorial Sloan Kettering Cancer Center (MSK) and The University of Texas MD Anderson Cancer Center (MDA). All patients with surgically staged endometrial carcinoma who were treated at MSK or MDA from January 1, 2009, through December 31, 2017, were retrospectively identified. Surgery consisted of hysterectomy and bilateral salpingectomy with or without oophorectomy or regional lymph node assessment. Open and minimally invasive surgical approaches were included. All patients had 2009 FIGO stage I disease. Endometrioid, serous, clear cell, carcinosarcoma, and undifferentiated/dedifferentiated histologies were included; cases of uterine sarcoma were excluded.

Patient characteristics, including age at surgery, body mass index (BMI), medical comorbidities, race, and ethnicity, were collected. Pathologic variables reviewed included histology, FIGO grade (endometrioid histology), depth of myometrial invasion, cytology, and presence of LVSI. HIR status was assigned per GOG-249 criteria – age ≤ 50 years with 3 risk factors, age 50–70 years with 2 risk factors, or age ≥ 70 years with 1 risk factor; risk factors included myometrial invasion ≥ 50%, grade 2 or 3 disease, and presence of LVSI [12]. Adjuvant treatment was given in accordance with National Comprehensive Cancer Network (NCCN) guidelines. Treatment options included no further therapy, chemotherapy alone, radiation alone, or a combination thereof. At both MSK and MDA, VBT is typically delivered 4 to 8 weeks postoperatively, with a total dose of 18 to 21 Gy administered in 3 fractions, or 30 Gy administered in 5 fractions. The dose is prescribed to a depth of 0.5 cm. The length of vagina treated ranges from 2.5 to 7 cm based on histology, with high-grade tumors treated up to 7 cm.

Clinical surveillance was routinely performed every 3 to 4 months in the first 2 years, and then every 6 months in subsequent years. These visits consisted of symptom assessment, gynecologic exam, and clinical imaging, when indicated.

Table 1
Clinical, surgical, pathologic, and treatment characteristics of patients with stage I endometrial carcinoma.

	Total Patients ($N = 2815$)
Age, years (range)	61 (26–92)
BMI, kg/m^2 (range)	31 (15–82)
Race/Ethnicity, n (%)	
White	2053 (73)
Black	205 (7)
Asian	177 (6)
Hispanic	340 (12)
Other/Unknown	40 (1)
Institution, n (%)	
MSK	2048 (73)
MDA	767 (27)
Medical Comorbidity Count, n (%)	
0–2	1606 (57)
3–5	516 (18)
> 5	693 (25)
Medical Comorbidities, n (%)	
Cardiovascular	1594 (30)
Endocrine	947 (18)
Gastrointestinal	436 (8)
Respiratory	336 (6)
Obesity	1592 (30)
Psychiatric	353 (7)
Histology, n (%)	
Endometrioid	2334 (83)
Serous	252 (9)
Clear cell	74 (3)
Carcinosarcoma	118 (4)
Undifferentiated/Dedifferentiated	37 (1)
Depth of Myometrial Invasion, n (%)	
0%	1328 (47)
< 50%	1175 (42)
≥ 50%	312 (11)
Endometrioid FIGO Grade, n (%)	
1	1331 (57)
2	785 (34)
3	218 (9)
Lymphovascular Space Invasion, n (%)	
Present	2226 (79)
Not present	581 (21)
Unknown	8 (0.3)
Cytology, n (%)	
Positive	183 (7)
Negative	1765 (63)
Unknown	867 (31)
Surgical Approach, n (%)	
Minimally invasive	2528 (90)
Open	287 (10)
Adjuvant Treatment, n (%)	
None	1705 (61)
VBT alone	557 (20)
VBT combination	403 (14)
Non-VBT based	150 (5)

BMI: body mass index; MSK: Memorial Sloan Kettering Cancer Center; MDA: The University of Texas MD Anderson Cancer Center; FIGO: The International Federation of Gynecology and Obstetrics; VBT: vaginal brachytherapy.

The primary outcome of this study was rate of isolated vaginal recurrence. Date of recurrence was determined by the clinical exam date with pathologic-confirmed biopsy or radiologic evidence resulting in further treatment. Clinical records were reviewed to identify descriptive anatomic location of recurrence within the vaginal vault. Extravaginal recurrence was defined in patients with metastatic disease irrespective of vaginal involvement. The vaginal apex was defined as the superior portion of the vagina suspended to the pelvic sidewall by cardinal and uterosacral ligaments [13].

Continuous variables were described using descriptive statistics and compared using the Mann-Whitney *U* test. Nonparametric categorical variables were assessed by chi-square or Fisher exact tests.

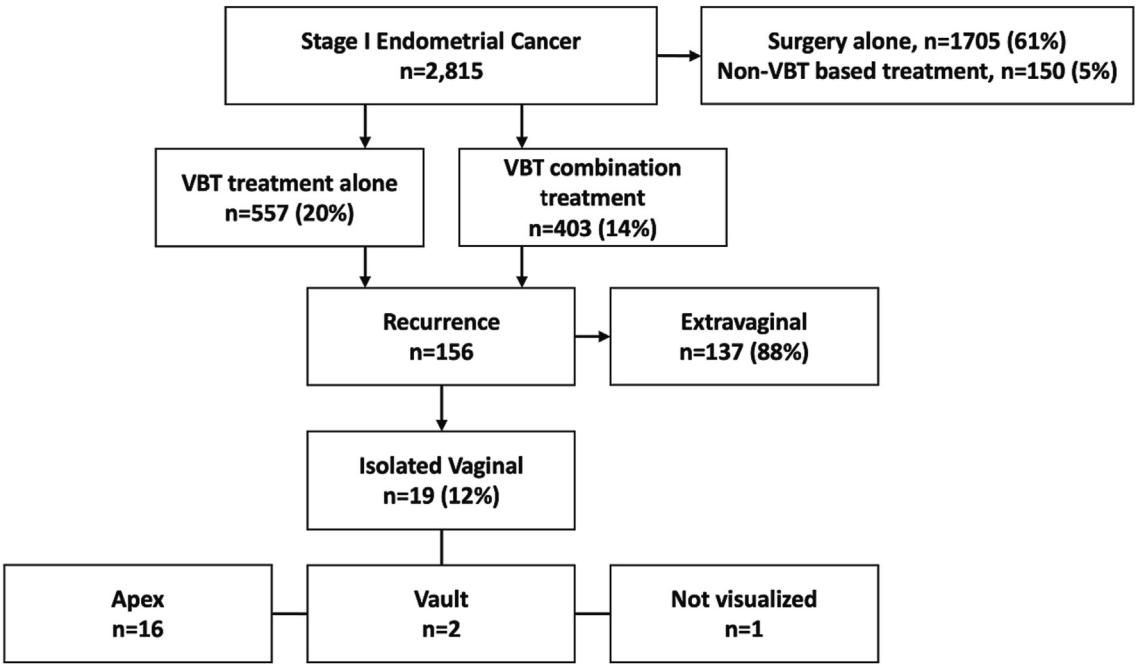

Fig. 1. Flow depiction of patients diagnosed with stage I endometrial carcinoma treated with vaginal brachytherapy (VBT) and characterization of isolated vaginal recurrence.

Progression-free survival (PFS) was measured from date of surgery to date of recurrence or last known follow-up. Overall survival (OS) was measured from date of surgery to date of death or last known follow-up. Outcome data analyses were performed using the Kaplan-Meier method and log-rank regression for comparison. *P* values < .05 were considered statistically significant. All statistics were performed with SPSS version 28.

3. Results

A total of 2815 women with stage I endometrial carcinoma were identified across both institutions. The median age at time of surgery was 61 years (range, 26–92 years), with a median follow-up of 38 months (range, 0.1–139 months). Our patient population was 73% White, 12% Hispanic, and 7% Black. Common medical comorbidities included cardiovascular (30%), endocrine (18%), and gastrointestinal (8%) disorders. The median BMI was 31 kg/m^2 (range, 15–82 kg/m^2), and 1592 patients (30%) were obese (BMI ≥ 30 kg/m^2; Table 1).

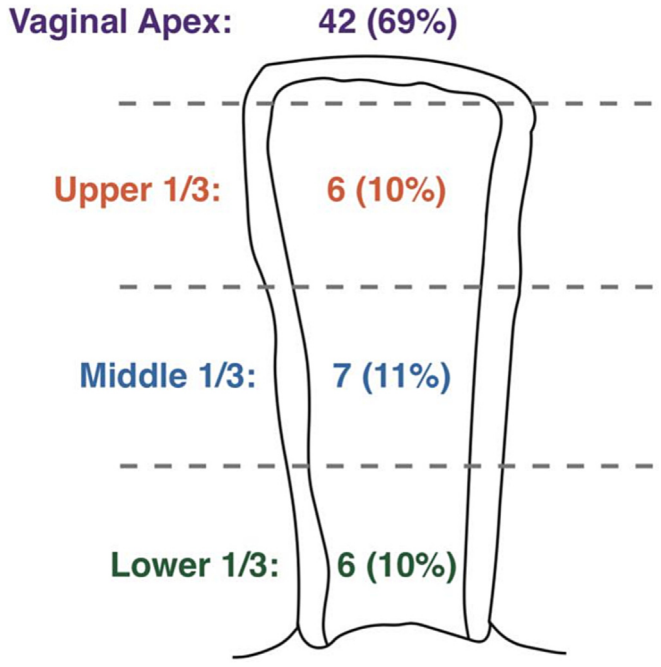

Fig. 2. Location of recurrence for the 61 women with stage I endometrial carcinoma in whom isolated vaginal recurrence was diagnosed.

Endometrioid histology was diagnosed in 2334 patients (83%), with serous and carcinosarcoma diagnosed in 252 patients (9%) and 118 patients (4%), respectively. Deep myometrial invasion (≥ 50%) was found in 312 patients (11%), LVSI in 2226 (79%), and positive cytology in 183 (7%). Of note, 867 patients (31%) did not have cytology collected. Adjuvant therapy was prescribed to 1110 patients (39%), with modalities including VBT alone (n = 557, 20%), VBT in combination with chemotherapy, EBRT, or both (n = 403, 14%), and non-VBT-based treatment (n = 150, 5%; Fig. 1). A total of 1705 patients (61%) did not receive any adjuvant treatment (Table 1).

Overall, 278 patients (10%) within our cohort experienced a recurrence, of whom 73 (26%) were in the VBT-alone group, 83 (30%) were in the VBT-combination group, 33 (12%) were in the non-VBT-based treatment group, and 89 (32%) were in the no adjuvant treatment group. Isolated vaginal recurrences (n = 61) were found in 13 of 73 patients (18%) in the VBT-alone group, 6 of 83 (7%) in the VBT-combination group, 4 of 33 (12%) in the non-VBT-based treatment group, and 38 of 89 (43%) in the no adjuvant treatment group. Recurrences at the apex (n = 42) were found in 10 of 13 (77%) patients in the VBT-alone group, 6 of 6 (100%) in the VBT-combination group, 2 of 4 (50%) in the non-VBT-based treatment group, and 24 of 38 (63%) in the no adjuvant treatment group. Extravaginal recurrences were found in the remaining 217 patients, 18 (8%) of whom experienced a concurrent vaginal recurrence.

Of the 61 isolated vaginal recurrences, 42 (69%) were located at the apex and 19 (31%) along the vaginal canal (Fig. 2). All but 2 isolated vaginal recurrences were clinically detected on exam; 1 (2%) was detected by imaging and 1 (2%) by Papanicolaou test. Compared to isolated vaginal recurrence, patients with extravaginal recurrence were more likely to have non-endometrioid histology (48% vs 15%, P < .01), endometrioid FIGO grade 3 disease (27% vs 2%, P < .01), and LVSI (45% vs 28%, P = .02), and to be categorized as HIR (49% vs 25%, P < .01). Patients who developed an isolated vaginal recurrence were more likely to

Table 2
Comparison of clinical, treatment, and pathologic characteristics between isolated vaginal and extravaginal recurrence groups.

	Isolated Vaginal Recurrence (n = 61)	Extravaginal Recurrence (*n* = 217)	*P* value
Age, years (range)	68 (30–89)	65 (37–92)	0.30
BMI, kg/m^2 (range)	31.1 (18.9–60.4)	31.9 (17.5–76.3)	0.23
Histology, n (%)			**<0.01**
Endometrioid	52 (85)	115 (53)	
Serous	3 (5)	47 (22)	
Clear cell	3 (5)	12 (6)	
Carcinosarcoma	3 (5)	39 (18)	
Undifferentiated/Dedifferentiated	0 (0)	4 (2)	
Depth of Myometrial Invasion, n (%)			0.08
0%	15 (25)	50 (23)	
< 50%	37 (61)	105 (48)	
≥ 50%	9 (15)	62 (29)	
Endometrioid FIGO Grade, n (%)			**<0.01**
1	24 (46)	24 (21)	
2	27 (52)	60 (52)	
3	1 (2)	31 (27)	
Lymphovascular Space Invasion, n (%)			**0.02**
Present	17 (28)	97 (45)	
Not present	44 (72)	119 (55)	
Unknown	0 (0)	1 (0.5)	
Cytology, n (%)			0.77
Positive	6 (10)	27 (12)	
Negative	34 (56)	124 (57)	
Unknown	21 (34)	66 (30)	
High-Intermediate Risk*, n (%)			**<0.01**
Positive	13 (25)	56 (49)	
Negative	39 (75)	59 (51)	
Adjuvant Treatment Type, n (%)			**<0.01**
VBT alone	13 (21)	60 (28)	
VBT combination	6 (10)	77 (35)	
Non-VBT based	4 (7)	29 (13)	
None	38 (62)	51 (24)	
Surgical Approach, n (%)			1.00
Minimally invasive	53 (87)	188 (87)	
Open	8 (13)	29 (13)	
Minimally Invasive Approach+, n (%)			0.15
Laparoscopy	35 (67)	143 (78)	
Robotic-assisted laparoscopy	17 (33)	41 (22)	
Medical Comorbidities, n (%)			0.22
0–2	30 (49)	116 (53)	
3–5	18 (30)	42 (19)	
> 5	13 (21)	59 (27)	

BMI: body mass index; FIGO: The International Federation of Gynecology and Obstetrics; VBT: vaginal brachytherapy.
* GOG-249 high-intermediate risk criteria: age ≤ 50 years with 3 risk factors, age 50–70 years with 2 risk factors, age ≥ 70 years with 1 risk factor; risk factors: myometrial invasion ≥ 50%, grade 2 or 3 disease, lymphovascular space invasion.
+ Removed cases with a combined robotic-assisted and traditional laparoscopic approach.

receive surgery alone as initial primary treatment (62% vs 24%, $P < .01$), while those with extravaginal recurrence were primarily treated with VBT (63% vs 31%, $P < .01$; Table 2). After initial endometrial carcinoma diagnosis, the median time to isolated vaginal recurrence was 11 months (range, 1–68 months) and to extravaginal recurrence was 20 months (range, 1–98 months; $P = .004$; Fig. 3).

When comparing all women in our cohort who received VBT-based treatment and either had an isolated vaginal recurrence ($n = 19$), extravaginal recurrence ($n = 137$), or no recurrence ($n = 804$), there were no significant differences in BMI, endometrioid grade, cytology, surgical approach, and medical comorbidities. VBT treatment with resultant extravaginal recurrence had a greater association with non-endometrioid histology (52% vs 32%–33%, $P < .01$), myoinvasion ≥ 50% (36% vs 24%–26%, $P = .049$), presence of LVSI (53% vs 41%–42%, $P = .04$), and HIR status (66% vs 36%–54%, $P < .01$; Table 3).

Minimally invasive surgery (MIS) was used in 2528 patients (90%) in our cohort. There was no association between surgical approach and recurrence location ($P = 1.00$; Table 2). From initial diagnosis to first recurrence, the 3-year PFS rate was 89.8% (SE +/− 0.7%) with MIS and 88.3% (SE +/− 2.0%) with open surgery ($P = .7$; Supplementary Fig. S1). The 3-year PFS rate for isolated vaginal recurrence was 97.6% (SE +/− 0.4%) with MIS and 96.9% (SE +/− 1.1%) with open surgery ($P = .8$; Supplementary Fig. S2A). The 3-year PFS rate for extravaginal recurrence was 91.8% (SE +/− 0.7%) with MIS and 90.8% (SE +/− 1.8%) with open surgery ($P = .8$; Supplementary Fig. S2B).

4. Discussion

To our knowledge, this is the largest collaborative study at two high-volume cancer centers to compare the location of recurrence within the vaginal vault in stage I endometrial carcinoma. We identified an overall recurrence rate of 10%, and a vaginal recurrence rate of 2%. Most recurrences occurred at the vaginal apex ($n = 42$, 69%; Fig. 2). While most patients with isolated vaginal recurrence did not receive any treatment, 19 (31%) had received VBT-based therapy. Despite VBT treatment, recurrence at the vaginal apex was found in 16 of 19 (84%) patients. Patients with an isolated vaginal recurrence were also more likely to recur within 1 year compared to those with extravaginal recurrence (median, 11 months vs 20 months, respectively). Given that 98% of patients with isolated vaginal recurrence were detected on physical exam, the value of clinical visits cannot be understated.

Current guidelines for adjuvant treatment of early-stage endometrial cancer primarily consider patient and pathologic risk factors,

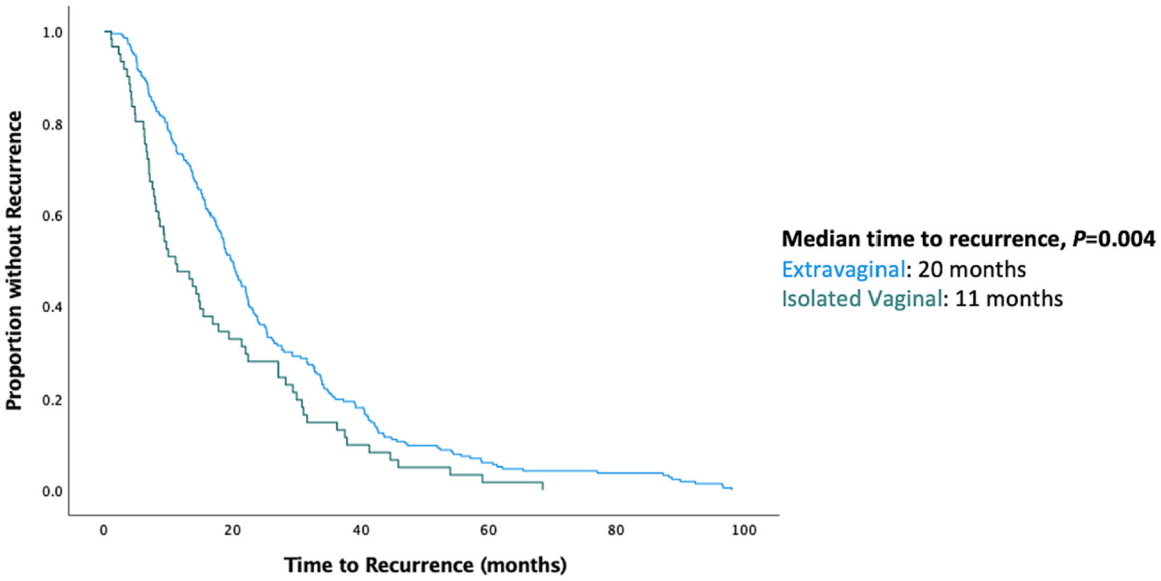

Fig. 3. Time to disease recurrence from initial diagnosis for patients with either extravaginal or isolated vaginal recurrence.

Table 3
Comparison of clinical, treatment, and pathologic characteristics between patients who received vaginal brachytherapy (VBT)-based treatment and resultant isolated vaginal recurrence, extravaginal recurrence, or no recurrence.

	VBT + Isolated Vaginal Recurrence (n = 19)	VBT + Extravaginal Recurrence (n = 137)	VBT + No Recurrence (n = 804)	P value
Age (range)	68 (50–89)	65 (46–90)	64 (26–92)	**0.03**
BMI, kg/m^2 (range)	30.8 (18.9–58.9)	31.4 (19.4–76.3)	30.7 (15.1–68.2)	1.00
Histology, n (%)				**<0.01**
Endometrioid	13 (68)	65 (47)	538 (67)	
Serous	3 (16)	33 (24)	139 (17)	
Clear cell	2 (11)	11 (8)	41 (5)	
Carcinosarcoma	1 (5)	25 (18)	59 (7)	
Undifferentiated/ Dedifferentiated	0 (0)	3 (2)	27 (3)	
Depth of Myometrial Invasion, n (%)				**0.049**
0%	3 (16)	23 (17)	147 (18)	
< 50%	11 (58)	65 (47)	468 (58)	
≥ 50%	5 (26)	49 (36)	189 (24)	
Endometrioid FIGO Grade, n (%)				0.29
1	5 (38)	10 (15)	187 (35)	
2	7 (54)	31 (48)	209 (39)	
3	1 (8)	24 (37)	142 (26)	
Lymphovascular Space Invasion, n (%)				**0.04**
Present	8 (42)	72 (53)	328 (41)	
Not present	11 (58)	64 (47)	471 (59)	
Unknown	0 (0)	1 (0.7)	5 (0.6)	
Cytology, n (%)				0.74
Positive	2 (11)	15 (11)	61 (8)	
Negative	11 (58)	82 (60)	499 (62)	
Unknown	6 (32)	40 (29)	244 (30)	
High-Intermediate Risk*, n (%)				**<0.01**
Positive	7 (54)	43 (66)	193 (36)	
Negative	6 (46)	22 (34)	345 (64)	
Surgical Approach, n (%)				0.42
Minimally invasive	15 (79)	122 (89)	694 (86)	
Open	4 (21)	15 (11)	110 (14)	
Minimally Invasive Approach+, n (%)				0.09
Laparoscopy	7 (47)	27 (23)	201 (30)	
Robotic-assisted laparoscopy	8 (53)	92 (77)	473 (70)	
Medical Comorbidities, n (%)				0.56
0–2	8 (42)	68 (50)	444 (55)	
3–5	4 (21)	26 (19)	148 (18)	
> 5	7 (37)	43 (31)	212 (26)	

BMI: body mass index; FIGO: The International Federation of Gynecology and Obstetrics; VBT: vaginal brachytherapy.

* GOG-249 high-intermediate risk criteria: age ≤ 50 years with 3 risk factors, age 50–70 years with 2 risk factors, age ≥ 70 years with 1 risk factor; risk factors: myometrial invasion ≥ 50%, grade 2 or 3 disease, lymphovascular space invasion.

+ Removed cases with a combined robotic-assisted and traditional laparoscopic approach.

including age, FIGO grade, histology, depth of myometrial invasion, and presence of LVSI. Early treatment paradigms included EBRT in patients with uterine-confined disease [4,14]. Compared to pelvic EBRT, VBT was subsequently shown to have no difference in oncologic outcomes and equivalent locoregional control [6]. GOG-249 was the first trial to include early-stage non-endometrioid histology in addition to endometrioid histology. The study examined combined VBT with chemotherapy against pelvic EBRT and found no significant differences in survival outcomes or rates of vaginal and distant recurrences; however, there were more extravaginal recurrences in the combined treatment arm (53 [18%; VBT with chemotherapy] vs 49 [16%; EBRT]) [12]. While the rates of isolated vaginal recurrences within these studies remain low, we sought to define recurrences by anatomic location within the vaginal vault and to identify treatment patterns in stage I endometrial carcinoma.

Our institutions follow surveillance strategies recommended by NCCN [2]. Early detection of recurrences has been shown to benefit overall outcomes due to improved treatment options [15]. While our study does not distinguish between patients with vaginal recurrence who were and were not symptomatic, all recurrences were confirmed on biopsy except for one, which was confirmed on clinically indicated imaging. Physical examination and patient education therefore remain paramount, even as telehealth is increasingly incorporated into clinical practice. Patients in our study who recurred were diagnosed with a variety of histologies; however, most had endometrioid with otherwise low-risk features. Surveillance methods for historically categorized type II endometrial carcinoma have included tumor marker testing, vaginal cytology, and imaging; although, these modalities have not been found to improve recurrence detection [16–18].

Delivery of VBT is an important consideration. While details regarding the dose rate, fractionation, length of vagina treated, and depth of vagina treated were not recorded in the current study, the range of accepted treatment parameters is well known [19–21]. Interestingly, 84% of patients who had an isolated recurrence at the vaginal apex had received VBT-based adjuvant therapy. Potential factors for recurrence may include vaginal cylinder displacement or varied dose distribution based on applicator positioning [22].

A recent study by Jensen et al. evaluated local control of endometrial carcinoma treated with 1 to 2 cm of active length as opposed to the American Brachytherapy Society's recommended length of 3 to 5 cm [23]. Patients treated with a cylinder length of 1 cm had significantly worse 5-year vaginal recurrence-free survival compared to those treated with a cylinder length of 2 cm [24]. The authors also found a significant difference in outcomes based on the immobilization technique of the applicator; improved survival was observed with use of a patient-mounted suspender device as opposed to the traditional table-mounted stand (5-year recurrence-free survival of 100% vs 86.7%, respectively; $P < .01$). These studies emphasize the importance of proper positioning of the vaginal applicator and of the patient, which may have a role in the pattern of recurrence.

When assessing outcomes by surgical approach, we found no association between PFS and MIS or PFS and open surgery. Additionally, 17% of patients in our study had high-risk endometrial cancer histology. Although this population was included in the LAP2 and LACE studies, no previous focused prospective studies have evaluated surgical approach in uterine-confined tumors in this high-risk population [25,26]. Our data support existing evidence of no difference in outcomes by surgical route in stage I endometrial carcinoma [27–30].

Strengths of this study include our robust medical record system, which allowed for detailed anatomical localization of recurrence within the vaginal vault. Another strength is our comprehensive approach to patient treatment, which included teams of gynecologic oncology surgeons, medical oncologists, and radiation oncologists. Limitations of our study include those inherent to retrospective study designs. The lack of detailed information on radiation therapy also limited our assessment of the effects of VBT on isolated vaginal recurrences. We also recognize treatment patterns and staging criteria changed throughout the study period, which likely contributed to variations in treatment. Differences in decisions made by treatment conferences or surgical approach may have also varied between institutions.

5. Conclusion

Patients with stage I endometrial carcinoma who experience a vaginal recurrence are more likely to be detected earlier than those who experience a non-vaginal recurrence. Identification of vaginal recurrences on physical exam highlights the importance of examining the vaginal apex throughout the early years of follow-up. Adjuvant treatment with VBT alone or in combination confers a 1% to 2% risk of isolated recurrence in the vagina. Most of the recurrences were found at the vaginal apex, which should be considered in future studies to optimize patient outcomes.

Consent Statement

This retrospective study was approved through a joint Institutional Review Board (IRB) submission at Memorial Sloan Kettering Cancer Center and The University of Texas MD Anderson Cancer Center, and all patients provided written consent.

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CRediT authorship contribution statement

Eric Rios-Doria: Conceptualization, Data curation, Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Han T. Cun:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Olga T. Filippova:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Jennifer J. Mueller:** Writing – original draft, Writing – review & editing. **Kaled M. Alektiar:** Writing – original draft, Writing – review & editing. **Lora H. Ellenson:** Writing – original draft, Writing – review & editing. **Vicky Makker:** Writing – original draft, Writing – review & editing. **Yulia Lakhman:** Writing – original draft, Writing – review & editing. **Mario M. Leitao:** Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Anuja Jhingran:** Writing – original draft, Writing – review & editing. **Pamela T. Soliman:** Conceptualization, Writing – original draft, Writing – review & editing. **Nadeem R. Abu-Rustum:** Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

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patent (adaptive intracavitary brachytherapy applicator for cervical cancer). The other authors do not have potential conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2023.10.011.

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