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Evolving trends in the management of high-intermediate risk endometrial cancer in the United States

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HIGHLIGHTS

- Management of high-intermediate risk endometrial cancer is controversial.
- GOG 249 aimed to define standard adjuvant treatment in these patients.
- We found that most women are not treated per either arm of GOG 249.
- The majority of women receive no adjuvant therapy following surgery.

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ABSTRACT

Objective. Gynecologic oncology group protocol 249 (GOG 249) is the contemporary US study that aimed to define the standard of care adjuvant therapy for patients with high-intermediate risk (HIR) endometrial cancer; patients were randomized to pelvic radiation therapy (RT) or vaginal brachytherapy (VBT) with chemotherapy (VBT-C). The preliminary results of GOG 249 were recently presented, yet the management of patients represented in this trial remains controversial. We set out to review US patterns of care for patients meeting eligibility criteria for GOG 249.

Methods. The National Cancer Database (NCDB) was used to identify patients meeting GOG 249 eligibility criteria between 2010 and 2015. The Man-Kendall trend test was used to assess for significant trends over time.

Results. We identified 23,015 patients that met study inclusion criteria. Between 2010 and 2015, there was a decline in the use of pelvic RT from 9.8% to 7.5%, although not meeting statistical significance ($p = 0.136$), and an increase in the use of VBT-C from 4.6% to 7.7% ($p = 0.017$). Most patients did not receive treatment per either arm of GOG 249, with observation being the most common approach throughout this era, although the percentage of patients observed decreased from 58.1% to 45.8% between 2010 and 2015 ($p = 0.003$). Further, 21.5% of patients received VBT alone in 2010, increasing to 30.3% by 2015 ($p = 0.003$).

Conclusions. National practice trends in HIR endometrial cancer reveal that a large number of patients are observed in lieu of receiving adjuvant therapy. Further, the utilization of pelvic RT has declined below utilization of VBT-C, despite a lack of data supporting either improved disease outcomes or toxicity with this experimental regimen on GOG 249.

1. Introduction

Endometrial carcinoma is the most common gynecologic malignancy in the developed world [1], and the vast majority of women present with early-stage disease limited to the uterine body. The backbone of management for early stage disease is total hysterectomy and bilateral salpingo-oopherectomy (BSO) with surgical staging with adjuvant treatment recommendations based on patient and tumor risk factors

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for recurrence. A series of studies have defined endometrial cancer risk groups and sought to identify optimal adjuvant management strategies based on these risk factors for recurrence.

The Gynecologic Oncology Group (GOG) 33 trial was a surgical-pathologic analysis that sought to elucidate known and potential risk factors for endometrial cancer recurrence in women with early stage disease [2]. GOG 99 further refined these criteria to define a group of high-intermediate risk (HIR) patients for recurrence for whom, when compared to no adjuvant treatment, adjuvant external beam pelvic radiation (pelvic RT) provided the largest absolute reduction of locoregional recurrence (LRR). HIR criteria in this study included those with early stage disease with moderate to poorly differentiated tumors, presence of lymphovascular invasion (LVSI), and outer third myometrial invasion; patients age 50 or greater with any two of the above risk factors or patients of age of at least 70 with any of the above risk factors. Pelvic nodal dissection was standardized in this trial, removing a source of bias. LRR in this trial in the HIR subgroup was 26% versus 6% in those receiving adjuvant pelvic RT versus no additional treatment (NAT), respectively, making adjuvant pelvic RT the standard treatment for HIR stage I-II patients [3]. The Post Operative Radiation Therapy in Endometrial Carcinoma (PORTEC-1) similarly found locoregional recurrence reduction with the use of pelvic RT in HIR women [4].

PORTEC 2 sought to investigate whether VBT would be as effective as pelvic RT in reducing vaginal recurrence in these patients, with less toxicity. The definition of HIR differed from the GOG definition with the following eligibility criteria: [1] age >60 with outer half myometrial invasion, and grade 1 or 2, or with <50% myometrial invasion and grade 3, or [2] FIGO 1988 stage IIA (endocervical glandular involvement only) which has been removed from current FIGO staging. In this multicenter randomized-controlled trial, patients were randomized to pelvic RT or VBT following TAH-BSO, with removal of clinically suspicious pelvic or para-aortic (PA) lymph nodes. The authors found that locoregional and distant control between the arms was equivalent, with less toxicity and superior quality of life in the VBT arm [5]. These findings led the authors to conclude that VBT should be the adjuvant treatment of choice for patients with HIR endometrial cancer.

Despite these results, adjuvant therapy for HIR patients remains controversial and careful patient selection is critical [6]. GOG 249 aimed to further define the standard of care of adjuvant therapy for patients with early-stage, HIR endometrial cancer, as defined by the previously outlined inclusion criteria for GOG 99 with outer half myometrial invasion rather than outer third. In this study, the authors compared adjuvant VBT plus chemotherapy (VBT-C) to pelvic RT, and found that toxicities and cumulative incidence of pelvic or PA nodal recurrence at 5 years was higher in the VBT-C arm as compared to the pelvic RT arm (9.2% versus 4.4%, respectively). Furthermore, grade 3 or higher adverse events were reported in 187 patients receiving VBT-C compared with 32 patients in the pelvic RT group [7]. The present study aims to examine patterns of care in adjuvant radiation utilization for women with early-stage, HIR endometrial cancer utilizing the National Cancer Database (NCDB).

2. Materials and methods

The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society [8]. It is a hospital-based registry that represents 70% of all cancer cases in the United States, drawing data from >1500 commission-accredited cancer programs. The data used in the study are derived from a de-identified NCDB file. The NCDB has established criteria to ensure the data submitted meet specific quality benchmarks. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology used or for the conclusions drawn from these data. The following NCDB analysis was performed with the approval of our local institutional review board.

We queried the de-identified NCDB file for all patients with endometrial cancer (primary site codes C540-543, C548-549, C559, and classification of invasive disease) of endometrioid, clear cell, or serous histology. GOG 249 eligibility criteria were defined per protocol and only patients meeting these criteria were included. These inclusion criteria are based on age and the following risk factors: outer half myometrial invasion, LVSI, and grade 2 or 3. All patients with stage I/II (occult) serous or clear cell histology were included, and patients with occult stage II endometrioid histology were included, regardless of risk factors. Stage II (occult) disease was defined as pT2. For patients with stage I endometrioid histology, eligibility was based on age. Patients over 70 were included with ≥1 risk factor, patients 51–70 were included with ≥2 risk factors, and patients 50 or younger were included only if they had all three risk factors. Our search was limited to patients diagnosed in 2010 or later when coding for LVSI was implemented. Cohort selection criteria are detailed in Fig. 1.

The Man-Kendall trend test is a non-parametric test used to test whether an increasing or decreasing monotonic trend exists. We used the Mann-Kendall trend test to assess whether trends in the percent of annual cases by group were significant over time, where the level of significance was defined as alpha equal to or <0.05. Logistic regression models were used to assess the association between patient and disease characteristics and treatment. Overall survival (OS) was examined using the Kaplan-Meier method with log-rank comparison. GraphPad Prism version 5.03 (GraphPad Software Inc., La Jolla, CA) was used for creation of Kaplan-Meier curves presented in the supplemental figure.

3. Results

We identified 23,015 patients for study inclusion who met GOG 249 inclusion criteria as outlined in Fig. 1. Adjuvant management strategies included pelvic RT, VBT-C, observation, chemotherapy only, VBT only, and pelvic RT and chemotherapy. Patient, demographic, and tumor characteristics for each adjuvant approach are shown in Table 1.

Across all centers, the most common adjuvant therapy following hysterectomy was observation, then VBT alone (50.8% and 25.6% of all patients, respectively). The percentage of patients observed after surgery decreased from 58.1% to 45.8% between 2010 and 2015 ($p = 0.003$), while the use of VBT alone increased from 21.5% to 30.3% over the same period ($p = 0.003$). Pelvic RT was the third most common adjuvant treatment approach, however its use decreased from 9.8% to 7.5% over the study period, although this decline did not meet statistical significance ($p = 0.136$). Over the study period, we observed an increase the use of VBT plus chemotherapy from 4.6% to 7.7% ($p = 0.017$). The use of chemotherapy only also increased over the study period from 4.1% to 6.4%, however this trend did not reach statistical significance ($p = 0.056$).

Among academic centers, observation was the most common adjuvant therapy strategy, however its use decreased from 54.3% to 41.7% ($p = 0.003$). As also seen across all centers, VBT alone was the second most common adjuvant therapy, with its use increasing over the study period from 24.2% to 34.3% ($p = 0.017$). Pelvic RT alone was the third most common adjuvant therapy strategies employed in academic centers, however its use decreased over the study period from 9.0% to 6.9%, but again not meeting statistical significance ($p = 0.272$). The use of VBT-C increased from 5.8% to 7.1% of patients treated in academic centers, although these findings also did not meet statistical significance ($p = 0.272$). Chemotherapy alone significantly increased from 4.9% to 7.6% ($p = 0.017$). The least common adjuvant therapy- pelvic RT plus chemotherapy- also increased over the study period from 1.8% to 2.4%, however this trend was not significant ($p = 0.272$).

Across community centers observation was also the most common adjuvant therapy strategy, however its use decreased over the study period from 60.9% to 48.8%. This trend was statistically significant ($p = 0.017$). Following observation, VBT alone was the second most utilized adjuvant treatment and its use statistically significantly increased over

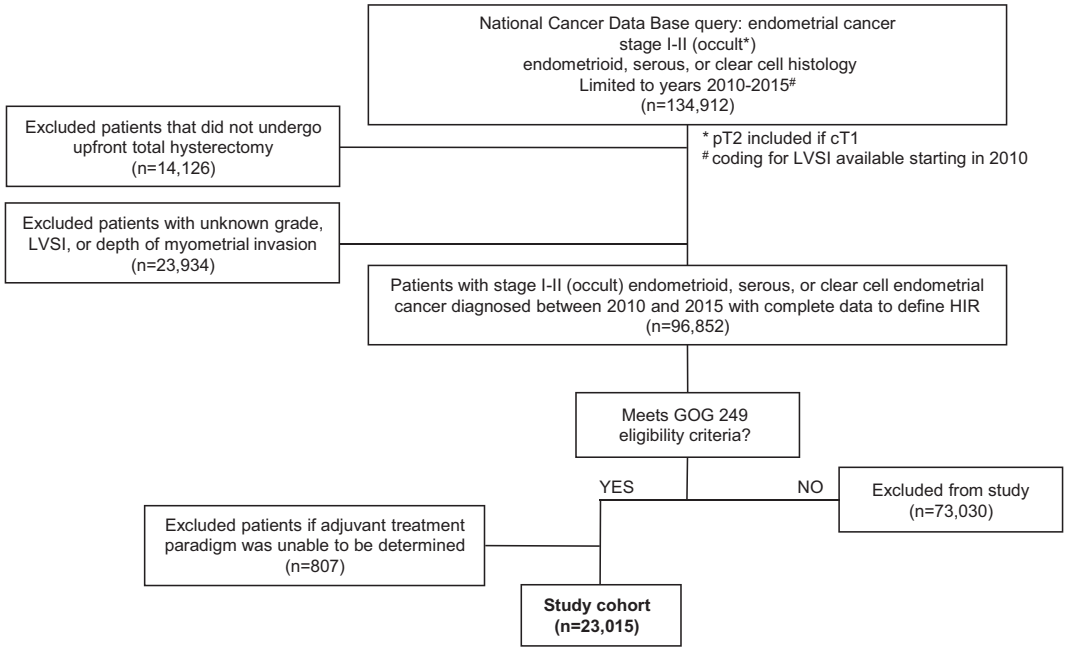

Fig. 1. Consort diagram illustrating patient cohort selection criteria. LVSI: lymphovascularspace invasion, HIR: high-intermediate risk, GOG: gynecologic oncology group.

Table 1
Patient characteristic. CDCC=Charlson/Deyo comorbidity score; LVSI = lymphovascular space invasion; Govt = government.

Variable	Pelvic RT	VBT and chemo	Observation	Chemo only	VBT only	Pelvic RT and chemo
Total patients	N = 2064	N = 1559	N = 11,694	N = 1287	N = 5902	N = 509
Age						
18–50	33 (2.1%)	33 (1.6%)	60 (0.5%)	22 (1.7%)	33 (0.6%)	17 (3.3%)
51–70	1201 (58.2%)	1073 (68.8%)	4014 (34.3%)	832 (64.6%)	3100 (52.5%)	364 (71.5%)
>70	830 (40.2%)	453 (29.1%)	7620 (65.2%)	433 (33.6%)	2769 (46.9%)	128 (25.1%)
CDCC						
0	1509 (73.1%)	1172 (75.2%)	8329 (71.2%)	964 (74.9%)	4352 (73.7%)	388 (76.2%)
1	432 (20.9%)	327 (21.0%)	2606 (22.3%)	252 (19.6%)	1246 (21.1%)	94 (18.5%)
2+	123 (6.0%)	60 (3.8%)	759 (6.5%)	71 (5.5%)	304 (5.2%)	27 (5.3%)
Race/ethnicity						
White (non-Hispanic)	1711 (82.9%)	1230 (78.9%)	9779 (83.6%)	912 (70.9%)	5123 (86.8%)	371 (72.9%)
Black	163 (7.9%)	175 (11.2%)	912 (7.8%)	241 (18.7%)	341 (5.8%)	80 (15.7%)
Hispanic	115 (5.6%)	76 (4.9%)	517 (4.4%)	61 (4.7%)	208 (3.5%)	37 (7.3%)
Other/unknown	75 (3.6%)	78 (5.0%)	486 (4.2%)	73 (5.7%)	230 (3.9%)	21 (4.1%)
Grade						
1	319 (15.5%)	98 (6.3%)	1886 (16.1%)	88 (6.8%)	1157 (19.6%)	30 (5.9%)
2/3	1745 (84.5%)	1461 (93.7%)	9808 (83.9%)	1199 (93.2%)	4745 (80.4%)	479 (94.1%)
LVSI						
No	962 (46.6%)	934 (59.9%)	8607 (73.6%)	855 (66.4%)	3527 (59.8%)	215 (42.2%)
Yes	1102 (53.4%)	625 (40.1%)	3087 (26.4%)	432 (33.6%)	2375 (40.2%)	294 (57.8%)
Outer half myometrial invasion						
No	311 (15.1%)	809 (51.9%)	5890 (50.4%)	798 (62.0%)	1708 (28.9%)	159 (31.2%)
Yes	1753 (84.9%)	750 (48.1%)	5804 (49.6%)	489 (38.0%)	4194 (71.1%)	350 (68.8%)
Histology						
Endometrioid	1971 (95.5%)	803 (51.5%)	10,513 (89.9%)	498 (38.7%)	5680 (96.2%)	320 (62.9%)
Clear cell/serous	93 (4.5%)	756 (48.5%)	1181 (10.1%)	789 (61.3%)	222 (3.8%)	189 (37.1%)
Insurance status						
None	49 (2.4%)	30 (1.9%)	214 (1.8%)	32 (2.5%)	98 (1.6%)	20 (3.9%)
Private	730 (35.4%)	662 (42.5%)	2862 (24.5%)	521 (40.4%)	2024 (34.3%)	225 (44.2%)
Medicaid/other govt	108 (5.2%)	81 (5.2%)	392 (3.4%)	69 (5.4%)	240 (4.1%)	33 (6.5%)
Medicare	1151 (55.8%)	777 (49.8%)	8118 (69.4%)	654 (50.1%)	3474 (58.9%)	225(44.2%)
Unknown	26 (1.3%)	8 (0.5%)	107 (0.9%)	10 (0.7%)	66 (1.1%)	6 (1.2%)
Median household income						
<$38,000	339 (16.4%)	215 (13.8%)	1397 (11.9%)	235 (18.3%)	767 (13.0%)	94 (18.5%)
$38–47,999	503 (24.4%)	327 (21.0%)	2667 (22.8%)	277 (21.5%)	1286 (21.8%)	111 (21.8%)
$48–62,999	555 (26.9%)	421 (27.0%)	3183 (27.2%)	330 (25.6%)	1550 (26.3%)	129 (25.3%)
>$63,000	663 (32.1%)	591 (37.9%)	3874 (33.1%)	443 (34.4%)	2292 (38.8%)	174 (34.2%)
Unknown	4 (0.2%)	5 (0.3%)	33 (0.3%)	2 (0.2%)	7 (0.1%)	1 (0.2%)
Distance to hospital						
<20 miles	1463 (70.9%)	1045 (67.0%)	7076 (60.5%)	831 (64.6%)	3804 (64.4%)	361 (70.9%)
>20 miles	596 (28.9%)	511 (32.8%)	4580 (39.2%)	453 (35.2%)	2090 (35.4%)	148 (29.1%)
Unknown	5 (0.2%)	3 (0.2%)	38 (0.3%)	3 (0.2%)	8 (0.1%)	0 (0.0%)

the study period from 19.6% to 27.5% ($p = 0.017$). Pelvic RT followed as the third most common adjuvant therapy in community centers, however its use decreased from 10.3% to 8.0% of patients being treated in community centers, and this trend approached statistical significance ($p = 0.056$). The use of VBT-C increased from 3.9% to 8.1%, a significant trend ($p = 0.003$). Chemotherapy alone in the adjuvant setting was uncommon, however its use increased from 3.7% to 5.6% ($p = 0.136$). Rarely, pelvic RT plus chemotherapy was employed, and its use increased marginally from 1.6% to 2.0% across community centers ($p = 0.719$); Fig. 2, Supplemental Table 1, Supplemental Table 2).

Under multivariate logistic regression, observation following surgery was associated with age older than 71 (odds ratio [OR] 1.688, CI 1.228–2.320, $p = 0.001$), Hispanic women (OR 1.189, CI 1.037–1.363), patients with CDCC scores 2 or higher (OR 1.233, CI 1.094–1.389, $p = 0.001$), uninsured women (OR 1.378, CI 1.129–1.682, $p = 0.001$) or those with Medicare (OR 1.091, CI 1.017–1.172, $p = 0.016$), and those living >20 miles from the treating hospital (OR 1.293, CI 1.217–1.373).

Factors associated with patients being less likely to be observed following surgery included serous or clear cell histology (OR 0.312, CI 0.285–0.342, $p < 0.001$), outer half myometrial invasion (OR 0.398, CI 0.373–0.426, $p < 0.001$), LVSI (OR 0.505, CI 0.474–0.537, $p < 0.001$), tumor grade 2/3 (OR 0.787, CI 0.726–0.854, $p < 0.001$), and median household income above $38,000 (Table 2).

We looked at Kaplan-Meier survival curves for patients stratified by treatment versus no treatment, and found that patients who received adjuvant treatment following hysterectomy had a statistically significant improvement in OS ($p < 0.001$, Supplemental Fig. 1).

4. Discussion

We know from previously mentioned studies that certain features such as deep myometrial invasion, high histologic grade, LVSI and stage of tumor correlate with a high-risk for recurrence. However, despite high-quality randomized evidence, the management of patients with early stage, HIR endometrial cancer remains varied across the country and practice types [9–11]. We reviewed patterns of care in the US for women eligible for the contemporary GOG study designed to define a standard adjuvant treatment strategy for these patients, and found that the vast majority of women were not treated per either arm of this study, and most commonly received no adjuvant therapy following surgery.

Observation remains an appropriate strategy for patients with early stage endometrial cancer with low to intermediate risk features, owing to low rates of recurrence following surgery, lack of demonstration of survival benefit with adjuvant therapy, and measurable toxicity with radiotherapy [12–16]. However, GOG 99 revealed that there is a subset of

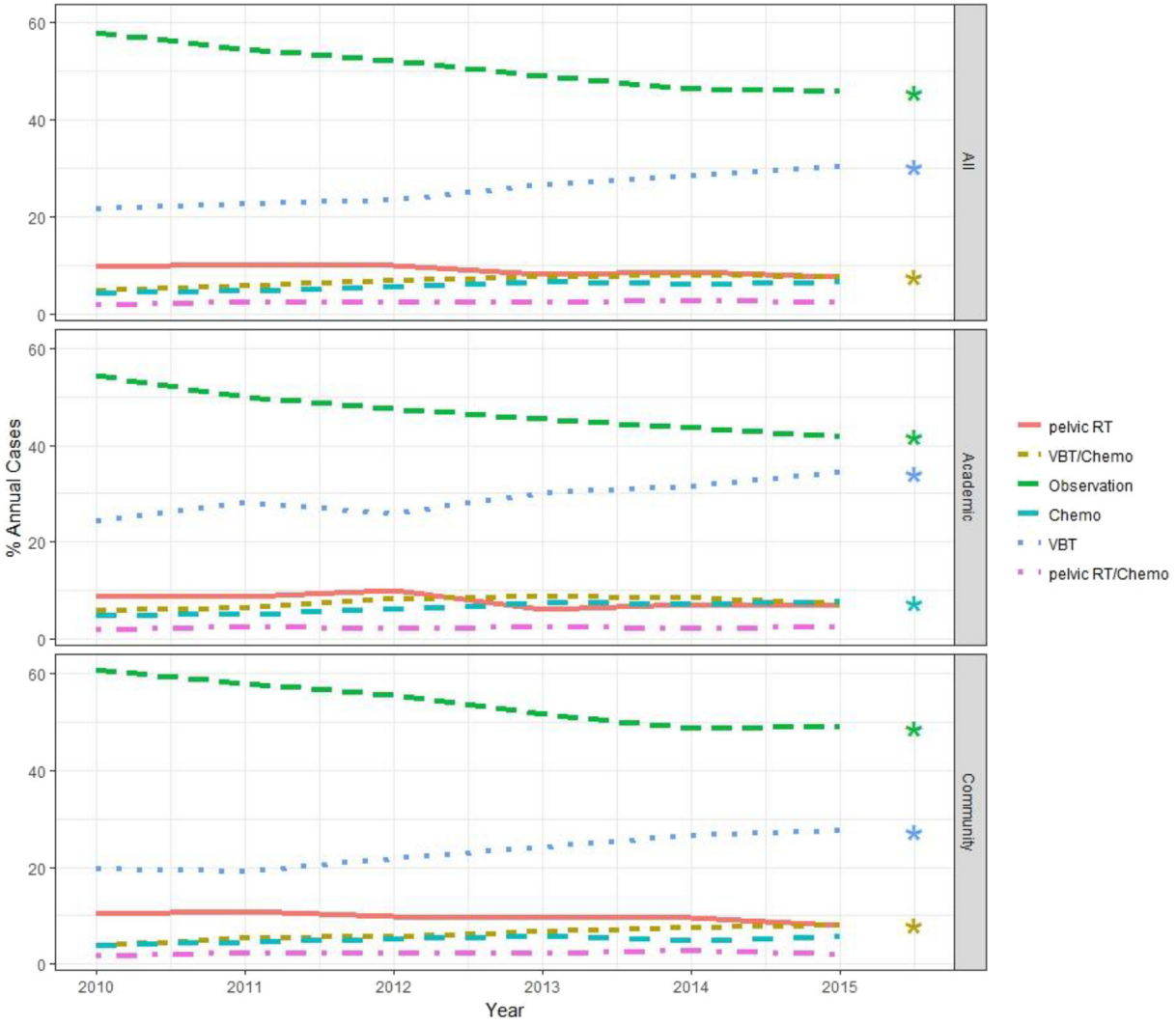

Fig. 2. Trends in the management of patients meeting eligibility criteria for gynecologic oncology group protocol 249 (GOG 249), shown by all cases, academic centers, and community centers. Asterisks denote a significant trend over time. RT: radiation therapy, VBT: vaginal brachytherapy, chemo: chemotherapy.

Table 2
Multivariate logistic regression evaluating odds ratio (OR) for not receiving adjuvant (adj) therapy following surgery. CI = Confidence Interval; CDCC = Charlson/Deyo comorbidity score; LVSI = Lymphovascular space invasion; Govt = Government.

	OR no adj therapy	p-Value	95% CI
Age			
18–50	*Ref*		
51–70	0.964	0.815	0.706–1.315
71+	1.688	0.001	1.228–2.320
Race/ethnicity			
Caucasian (non-Hispanic)	*Ref*		
Black	0.972	0.601	0.874–0.081
Hispanic	1.189	0.013	1.037–1.363
Other	1.159	0.037	1.009–1.332
CDCC			
0	*Ref*		
1	1.049	0.167	0.980–1.123
2	1.233	0.001	1.094–1.389
Histology			
Endometrioid	*Ref*		
Serous/clear cell	0.312	<0.001	0.285–0.342
Outer half myometrial invasion			
No	*Ref*		
Yes	0.398	<0.001	0.373–0.426
LVSI			
No	*Ref*		
Yes	0.505	<0.001	0.474–0.537
Tumor grade			
Grade 1	*Ref*		
Grade 2/3	0.787	<0.001	0.726–0.854
Insurance status			
Private	*Ref*		
Uninsured	1.378	0.001	1.129–1.682
Medicaid/other govt	1.016	0.826	0.878–1.176
Medicare	1.091	0.016	1.017–1.172
Unknown	1.087	0.560	0.821–1.440
Median household income			
<$38,000	*Ref*		
$38,000 – $47,999	0.873	0.004	0.796–0.957
$48,000 – $62,999	0.910	0.041	0.832–0.996
≥$63,000	0.810	<0.001	0.740–0.885
Distance to hospital			
<20 miles	*Ref*		
≥20 miles	1.293	<0.001	1.217–1.373

women with HIR features for recurrence who benefit significantly from the addition of pelvic RT. Nevertheless, the use of pelvic RT in HIR patients remains relatively uncommon and was used as adjuvant treatment in just 9.8% of HIR patients in 2010 and 7.5% of patients in 2015 in the present analysis.

Concurrent with the decline in use of pelvic RT, the use of VBT alone has statistically significantly increased over time, used as adjuvant treatment in 21.5% and 30.3% of women in 2010 and 2015, respectively ($p = 0.003$), perhaps owing to a favorable toxicity profile as demonstrated by PORTEC 2, as well as several other retrospective reports [5,17–25]. While we found no clear singular event that lead to the rise in utilization of VBT alone over the study period, in the years following the publication of PORTEC 2, the rate of increase in utilization of VBT alone went up as demonstrated in Fig. 2. Furthermore, VBT alone was the second most common adjuvant treatment strategy among patients in both community and academic centers, although the proportion of patients receiving VBT alone was higher in academic centers. The reason for this observation is unclear but may, in part, be due to regional practice variations or referral patterns from the community to high-volume centers with significant brachytherapy experience [26].

GOG 249 included slightly higher risk patients than those in PORTEC 2, who perhaps would not have had acceptable disease control outcomes with VBT alone. In GOG 249, VBT with the addition of chemotherapy was compared to pelvic RT following surgery. Following their initial late-breaking abstract at SGO in 2014, the authors proposed that VBT-C was not superior to pelvic RT in terms of recurrence free survival (84% versus 82%; HR 0.97) or OS (93% versus 92%). Interestingly, the use of VBT-C has significantly increased in the community over time despite these findings, from 3.9% to 8.1% ($p = 0.003$) during the study period, despite increased toxicity as compared to pelvic RT with the addition of chemotherapy to VBT. In academic centers, the use of VBT-C increased from 2010 to 2014, and subsequently decreased from 2014 to 2015 (not statistically significant), perhaps due to the initial presentation of results from GOG 249 in 2014. Furthermore, the recently updated presentation of GOG 249 findings in 2017 demonstrated that the cumulative incidence of pelvic and para-aortic nodal recurrence in the VBT-C arm of their trial was twice that of the pelvic RT arm (9.2% versus 4.4%, respectively). The authors concluded that adjuvant pelvic RT should remain the standard of care for high-risk, early-stage endometrial cancer; however, VBT remains increasingly common in the adjuvant setting [26–28]. These findings may continue to shift centers away from VBT-C in the coming years. Therefore, as we await additional data, adjuvant treatment in HIR women remains a moving target.

While we found that HIR criteria such as LVSI, outer half myometrial invasion, high tumor grade and high risk histology are independently associated with the receipt of adjuvant treatment compared to women without these features, 50% of women in the present study with HIR disease received no adjuvant treatment, independent of year or facility type. This same trend has been echoed in a large SEER analysis following the publication of PORTEC 2 [28] and persists despite randomized trials demonstrating a benefit to adjuvant pelvic RT following surgery in women with HIR disease. The finding is especially surprising in light of clear recommendations from ASTRO for the use of adjuvant radiation therapy in patients with HIR disease as defined in prior GOG and PORTEC studies. In their 2014 consensus guidelines, VBT was recommended for patients with grade 1 or 2 cancers with ≥50% myometrial invasion or grade 3 tumors with <50% myometrial invasion. Pelvic RT was recommended for women with grade 3 cancer with >50% myometrial invasion or cervical stromal invasion, as well as in patients suitable for VBT, above, with additional risk factors such as age > 60 and LVSI [29]. In practice, however, VBT may still be employed in women for whom pelvic RT is appropriate per the ASTRO guidelines, and is in fact deemed a potentially better option in patients who underwent adequate surgical staging per ASCO's endorsement and critique of those guidelines [30].

Despite these consensus recommendations for adjuvant therapy, women are most commonly being observed, the majority of whom are 70 and older, despite age being a HIR criterion in the several large cooperative group studies previously mentioned. The reasons for this observation are likely multifactorial. Fader et al. additionally found that in the United States, women with endometrial cancer older than age 70 are 50% less likely than their younger counterparts to receive adjuvant treatment after surgery despite worse prognosis based on age [31].

As with all retrospective analyses, our findings are subject to inherent selection biases. While the NCDB includes CDCC scores as a validated surrogate for patient comorbidities [32], it does not capture specific comorbidity information. Therefore, it is possible that the majority of patients in the present study, namely those aged 70 and older, were not offered adjuvant therapy or were not candidates for pelvic RT following surgery due to underlying medical comorbidities, postoperative complications, or wound healing issues. Additionally, pelvic RT, given over the course of several weeks, is logistically challenging for many patients and may not be feasible. Despite these limitations, the NCDB is a highly quality-controlled resource that captures information on approximately 70% of cancer cases diagnosed in the US, including approximately 77% of uterine cancer cases [33]. This makes it a well-suited resource for evaluating patterns of care among patients with endometrial cancer, as in the present study, across a diverse patient population [8].

Previous prospective randomized trials such as PORTEC 1 and GOG 99, which compared observation to pelvic RT in the adjuvant setting, failed to demonstrate improved overall survival with the addition of adjuvant therapy. Due to low number of events in this patient population,

neither of these trials were powered to demonstrate an overall survival benefit. Albeit subject to the limitations of retrospective selection bias, we did observe a survival advantage to adjuvant therapy in this cohort limited to HIR patients. This is likely due to the robust number of patients with HIR endometrial cancer captured by the NCDB, lending power to the present analysis [3,4].

The present study is timely in light of the 2014 and 2017 presentations of GOG 249 data recommending pelvic RT as a standard adjuvant treatment in women with HIR endometrial cancer. We have found that the majority of women are not treated per either arm of this study, and are actually observed following definitive surgery. This is despite GOG 99 demonstrating that adjuvant pelvic RT benefits women with HIR disease, significantly decreasing their chances of locoregional recurrence as compared to patients without high risk features. It is our hope that this study will increase awareness of adjuvant treatment patterns in the United States and lack of utilization of adjuvant radiation for appropriately selected patients, which is likely detrimental to optimal patient outcomes.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2018.12.010.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

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Conception and design: Sara J. Zakem, Tyler P. Robin, Christine M. Fisher

Provision of study materials or patients: Arya Amini

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Manuscript writing: All authors.

Final approval of manuscript: All authors.

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