Therapeutic Benefit of Radiotherapy in Uterine Serous Carcinoma (USC): A Real-World Study

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Background

- Approximately 10% of all endometrial cancers (ECs) are uterine serous (USC).[1]
- Distribution of stage at diagnosis is predominantly stage I (40%), followed by stage II (30%), stage III (20%), and stage IV (10%).[2]
- However, due to its aggressive nature, USC EC is associated with high recurrence and poor prognosis, and it accounts for 40% of EC-related deaths.[2]
- Treatment of EC may consist of multiple components.
  - Adjuvant chemotherapy (C) with carboplatin + paclitaxel is always recommended.
  - Surgery recommendations depend on diagnosis (e.g., total hysterectomy, bilateral salpingo-oophorectomy, etc.).
  - The benefit of adjuvant radiotherapy (vaginal brachytherapy or external beam radiotherapy [EBRT]) is currently unclear.
- Since the potential benefit and optimal timing of adjuvant radiotherapy is unclear additional real-world evidence is needed to understand its effectiveness.

Objective

- **The objectives were: i) To compare outcomes (overall (OS) and progression free (PFS) survival) in USC patients receiving only chemotherapy (C) and chemotherapy with External Beam Radiotherapy (EBRT) and ii) to assess the impact of timing of EBRT relative to C on patient outcomes.**

Methods

- Retrospective observational cohort study where patients with USC receiving:
  - C or C + adjuvant external beam radiotherapy (EBRT)
- All patients were treated at the McGill University Health Center (MUHC) between 2008 and 2023.
- Patient treatment characteristics and outcomes were ascertained from the MUHC Electronic Health Records and the MUHC Gyno-Oncology Database.
- Multivariable cox regression analyses were performed to understand the association between covariates and the outcomes of interest.

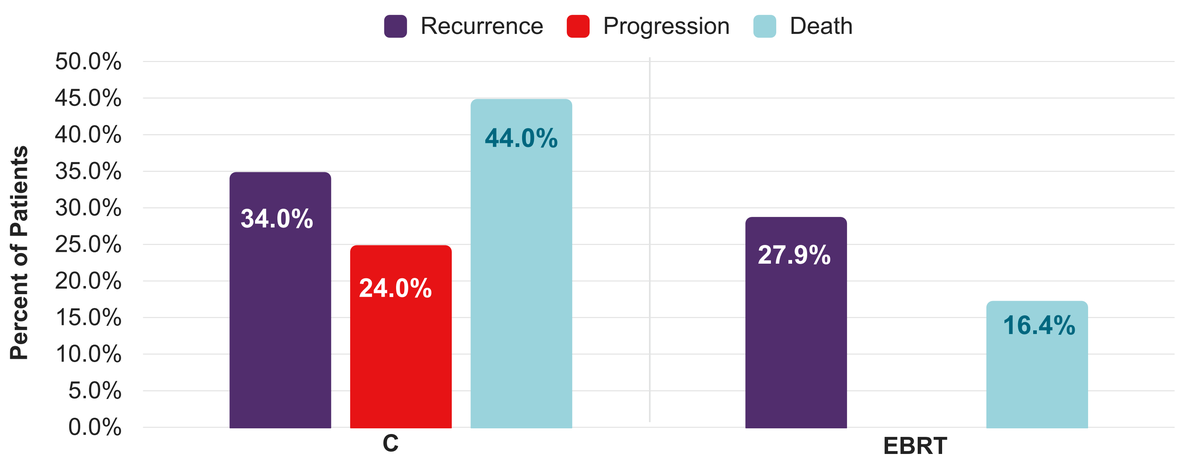
Results

Table 1. Patient characteristics and outcomes

		Treatment Group				*P*-value
		C (n=50)		C+EBRT (n=61)		
Mean (SD) age, years		67.30	(9.07)	69.40	(8.11)	0.219
Stage I		13	26.0%	31	50.1%	<0.001
Stage II		0	0.0%	13	21.3%	
Stage III		13	26.0%	16	26.2%	
Stage IV		24	48.0%	1	1.6%	
Preop albumin	< 3.5	6	12.0%	1	1.6%	0.028
Cytology	Malignant	23	46.0%	9	14.8%	<0.001
MMR Status	Deficient	1	2.0%	7	11.5%	0.046

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; MMR = mismatch repair status

Figure 1. Proportion of patients with clinical outcomes



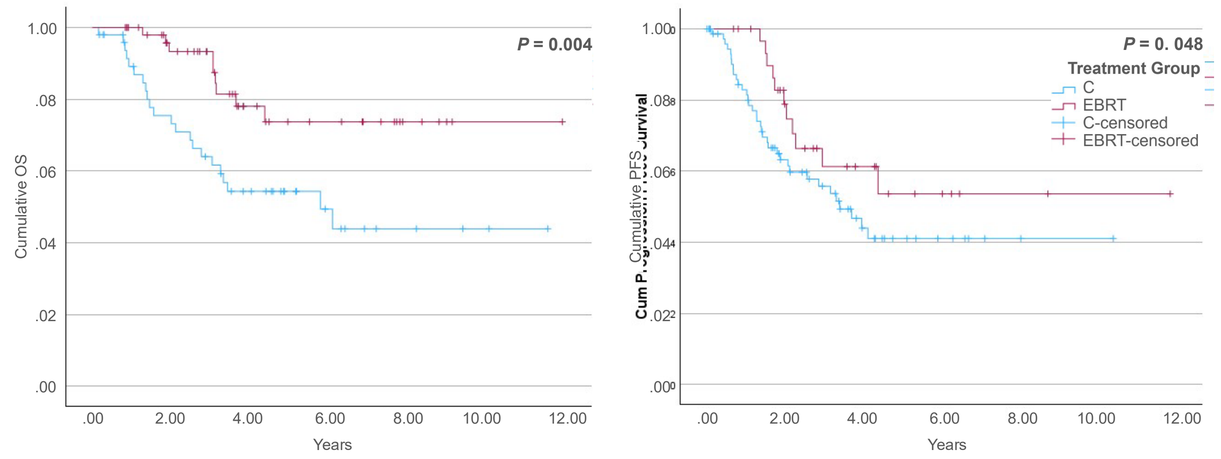
	Treatment Group				*P*-value
	C (n=50)		C+EBRT (n=61)		
Recurrence	17	34.0%	17	27.9%	0.560
Progression	12	24.0%	0	0.0%	<0.001
Death	22	44.0%	10	16.4%	0.005

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy

Results (cont.)

Cumulative OS and PFS

Figure 2. Cumulative OS and PFS



Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; OS= overall survival; PFS = progression-free survival

Regression Analyses

Table 2. Cox regression analyses understanding how covariates associate with clinical outcomes

	OS				PFS			
			95.0% CI for HR				95.0% CI for HR	
	P-value	HR	Lower	Upper	*P*-value	HR	Lower	Upper
EBRT vs C	0.242	0.571	0.223	1.459	0.141	0.584	0.285	1.196
Stage (III–IV) vs (I–II)	0.040	2.726	1.046	7.109	0.004	2.915	1.403	6.053
Pre-Op Albumin ≤ 3.5	0.685	1.362	0.306	6.056	0.926	0.934	0.218	4.004
MMR Deficient	0.978	0.000	0.000	—	0.389	0.531	0.126	2.242

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; HR = hazard ratio; MMR = Mismatch Repair; OS = overall survival; PFS = progression free survival

Table 3. Cox regression analyses including time to chemotherapy, understanding how covariates associate with clinical outcomes

	OS				PFS			
			95.0% CI for HR				95.0% CI for HR	
	P-value	HR	Lower	Upper	*P*-value	HR	Lower	Upper
Age	0.003	1.268	1.085	1.481	0.082	1.056	0.993	1.123
Stage (III–IV) vs (I–II)	0.653	1.515	0.248	9.257	0.045	3.054	1.023	9.117
Time to Chemotherapy	0.007	1.061	1.016	1.107	0.043	1.025	1.001	1.049
Time to EBRT	0.679	0.996	0.979	1.014	0.234	0.994	0.983	1.004

Abbreviations: EBRT = external beam radiotherapy; HR = hazard ratio; OS = overall survival; PFS = progression free survival
Time to event outcomes are assessed in days

Discussion

- Adjuvant radiation provided OS and PFS benefits for patients with USC EC.
- Delaying chemotherapy versus EBRT was associated with increased risk of mortality and recurrence.

Limitations

- This was a single-site study conducted in a tertiary center that is highly specialized in the treatment of gynecological cancers:
  - This study may not be representative of the general population with USC EC.
- This study was conducted in Canada (universal, publicly funded healthcare system).
  - Results may be different in non-public/universal healthcare systems, where access to care may be a barrier to receiving radiation therapy.
- The study was conducted prior to increased use of targeted and immunotherapy.
  - Thus, results may vary among inpatients treated with advanced therapies.

Conclusions

- **Adjuvant radiation therapy (EBRT) may be beneficial in patients with USC**
- **In these patients, chemotherapy should be initiated prior to radiotherapy to optimize treatment benefits.**
- **Real-world studies are required for cost-effectiveness treatment assessments.**
  - **Evidence from these studies will drive decisions regarding optimal use of high-cost treatments for rare diseases and cancers.**

References

1. Bogani G, et al. *Gynecol Oncol.* 2021;162(1):226-34. 2. Ball A, et al. *J Obstet Gynaecol Can.* 2014;36(12):1085-92.

Disclosures

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