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## Disparities in care for elderly women with endometrial cancer adversely effects survival

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### HIGHLIGHTS

- Elderly endometrial cancer patients are less likely to undergo adjuvant radiotherapy.
- In the elderly, 94% had oncologic surgery, but only 36% had adjuvant radiotherapy.
- Adjuvant radiotherapy is associated with improved survival in the elderly.
- Receipt of radiotherapy is excessively affected by demographic factors.
- Receipt of oncologic surgery is dependent on different demographic factors.

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### ABSTRACT

**Purpose.** Elderly women with endometrial cancer are at increased risk of local recurrence and cancer-specific death compared to younger women. We sought to investigate adjuvant radiotherapy (RT) practice patterns and effects on survival in elderly women with endometrial cancer.

**Methods.** Women from the National Cancer Data Base (NCDB) with FIGO IA grade 3 to FIGO IVA endometrial cancer diagnosed from 2004–2013 were included. Chi square analysis was used to compare the elderly (80+) and non-elderly women (18–79) and women who received RT and those that did not. Univariate and multivariate logistic regression were used to determine predictors of receipt of oncologic surgery and adjuvant RT. Univariate and multivariate Cox survival analyses were performed to examine the effect of radiotherapy on survival. Propensity score matching and shared frailty analysis were done in the elderly cohort.

**Results.** We identified 48,871 women for analysis. Rates of oncologic surgery were higher in the women 80+ compared with rates of adjuvant RT (95% versus 34%). Rates of RT receipt were higher in non-elderly women (48% versus 34%,  $p < 0.001$ ). Age over 80 was a negative predictive factor (OR 0.62,  $p < 0.001$ ) for receipt of adjuvant RT and oncologic surgery (OR 0.81,  $p = 0.03$ ). Adjuvant RT was associated with a decreased risk of death in elderly (HR 0.79,  $p < 0.001$ ) and non-elderly women (HR 0.77,  $p < 0.001$ ).

**Conclusion.** Endometrial cancer patients over age 80 have similar rates of oncologic surgery as younger women but are significantly less likely to receive adjuvant RT, and this negatively impacts their survival.

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### 1. Introduction

Endometrial cancer is the most common gynecologic malignancy in developed countries, presenting at a mean age of 60 [1]. Increasing age is a risk factor for more aggressive histology and grade, leading to increased loco-regional recurrence risk and decreased cancer-specific survival [2–10]. Older women tend to present at earlier stages where a cure is possible with appropriate treatment [2–4]. These factors together

favor treatment with standard of care surgery and adjuvant radiotherapy as needed. However, advanced age is associated with under-treatment in various female malignancies, including endometrial cancer [11–14].

The standard of care treatment for endometrial cancer in post-menopausal women is a minimally-invasive hysterectomy followed by adjuvant radiotherapy and/or chemotherapy in appropriately selected populations [4,12]. Evidence-based guidelines have been published in both North America and Europe for adjuvant radiotherapy in both early stage and locally advanced endometrial cancer [15–17]. Stage IA endometrioid tumors that are grade 1 or 2 without other risk features such as lymphovascular space invasion (LVSI) are considered low risk

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**Table 1**  
Comparison demographic, tumor, and treatment characteristics of elderly (80+) and non-elderly women (18–79) with endometrial cancer.

	Non-Elderly (43,432)	Elderly (5439)	p Value
<b>Race</b>			<b>p &lt; 0.001</b>
White	35,767 (83%)	4926 (92%)	
Black	3393 (8%)	260 (5%)	
Hispanic	2276 (5%)	124 (2%)	
Other	1524 (4%)	67 (1%)	
<b>Charlson</b>			<b>p &lt; 0.001</b>
0	32,582 (75%)	3913 (72%)	
1	8789 (20%)	1190 (22%)	
2+	2061 (5%)	336 (6%)	
<b>Facility type</b>			<b>p &lt; 0.001</b>
Community	2718 (6%)	399 (7%)	
Comprehensive community	19,338 (46%)	2664 (49%)	
Academic	17,278 (41%)	1953 (36%)	
Integrated	3156 (7%)	415 (8%)	
<b>Census region</b>			<b>p = 0.009</b>
Northeast	9328 (22%)	1211 (22%)	
South	14,430 (34%)	1717 (32%)	
Midwest	11,949 (28%)	1625 (30%)	
West	6859 (16%)	886 (16%)	
<b>Income (zip code)</b>			<b>p = 0.004</b>
Less than 30,000	5388 (13%)	595 (11%)	
30,000–34,999	7678 (18%)	932 (18%)	
35,000–45,999	11,854 (28%)	1553 (30%)	
46,000+	16,917 (40%)	2176 (41%)	
<b>% Residents without HS diploma</b>			<b>p &lt; 0.001</b>
29%+	6699 (16%)	682 (13%)	
20–28.9%	9722 (23%)	1197 (23%)	
14–19%	10,337 (25%)	1350 (26%)	
Less than 14%	15,076 (36%)	2027 (39%)	
<b>Distance to treatment facility</b>			<b>p &lt; 0.001</b>
Less than 50 miles	36,321 (85%)	4657 (87%)	
50–200 miles	6038 (14%)	629 (12%)	
Greater than 200 miles	578 (1%)	62 (1%)	
<b>Urban density</b>			<b>p = 0.01</b>
Metro	33,843 (81%)	4292 (82%)	
Urban	5478 (13%)	611 (12%)	
Rural	2682 (6%)	319 (6%)	
<b>Insurance status</b>			<b>p &lt; 0.001</b>
Private insurance	20,873 (49%)	484 (9%)	
No insurance	1912 (4%)	16 (<1%)	
Medicaid	2672 (6%)	76 (1%)	
Medicare	17,384 (41%)	4803 (89%)	
<b>FIGO stage</b>			<b>p &lt; 0.001</b>
IA	4427 (10%)	417 (8%)	
IB	17,389 (40%)	2748 (51%)	
II	9207 (21%)	991 (18%)	
IIIA	1453 (3%)	169 (3%)	
IIIB	764 (2%)	150 (3%)	
IIIC	9687 (22%)	889 (16%)	
IVA	505 (1%)	75 (1%)	
<b>Tumor size</b>			<b>p &lt; 0.001</b>
2 cm or less	4549 (15%)	492 (13%)	
2.1 cm–5 cm	16,528 (53%)	2353 (60%)	
Greater than 5 cm	10,066 (32%)	1049 (27%)	
<b>Grade</b>			<b>p &lt; 0.001</b>
Grade 1	10,614 (24%)	1186 (22%)	
Grade 2	17,499 (40%)	2187 (40%)	
Grade 3	14,333 (33%)	1898 (35%)	
Grade 4 (undifferentiated)	986 (2%)	168 (3%)	
<b>Lymph node surgery</b>			<b>p &lt; 0.001</b>
No	6637 (15%)	1512 (28%)	
Yes	36,679 (85%)	3913 (72%)	
<b>Number of lymph nodes removed</b>			<b>p &lt; 0.001</b>
10 or less	19,428 (46%)	3338 (65%)	
More than 10	22,544 (54%)	24,493 (35%)	
<b>Surgery type</b>			<b>p = 0.02</b>
Non-oncologic	1598 (4%)	234 (4%)	
Oncologic	41,833 (96%)	5205 (95%)	
<b>Chemotherapy</b>			<b>p &lt; 0.001</b>
No chemotherapy	26,098 (72%)	3840 (89%)	
Adjuvant chemotherapy	10,180 (28%)	481 (11%)	
<b>Radiotherapy</b>			<b>p &lt; 0.001</b>

**Table 1 (continued)**

	Non-Elderly (43,432)	Elderly (5439)	p Value
No radiotherapy	22,762 (52%)	3610 (66%)	
Radiotherapy	20,670 (48%)	1829 (34%)	
<b>Radiotherapy modality</b>			<b>p &lt; 0.001</b>
External beam	7807 (38%)	761 (42%)	
Brachytherapy	7391 (36%)	670 (37%)	
Beam & brachytherapy	5472 (26%)	398 (22%)	

Abbreviations: HS = high school; FIGO = International Federations of Gynecology and Obstetrics; cm = centimeter.  
Bold values are statistically significant at  $p < = 0.05$ .

for recurrence and do not require post-operative therapy [11,12]. All others are considered high-intermediate or high risk (Stage IA, grade 3 to Stage IVA), for which adjuvant therapy is an option, whether it is radiotherapy, chemotherapy or both [17,11,12]. Radiotherapy can be delivered to the vaginal cuff alone (vaginal cylinder brachytherapy) or the upper vagina and lymph nodes (whole pelvis) and is generally well-tolerated in elderly populations [15,16,18–22].

Large database studies, single institution studies [23], and literature reviews have examined the question of adjuvant radiotherapy use and outcomes in elderly women with both early and advanced endometrial cancer [24–27]. Though no large, randomized clinical trials have found a survival benefit of radiotherapy in endometrial cancer, a local recurrence benefit has consistently been observed. There is a suggestion in large database studies that this may translate to small gains in overall survival [24,26,27]. Regardless, local recurrences in the pelvis can be morbid and affect quality of life.

We hypothesized that “elderly” women (80 and over) with high-intermediate risk and high-risk endometrial cancer, who may be at higher risk for local recurrence and decreased cancer-specific survival, would be overall less likely to be treated with curative intent, as demonstrated in other studies [11–14]; though we expected that clinical and tumor characteristics alone would play the dominant role. We also sought to examine whether omission of radiotherapy in high-grade stage IA thru stage IVA patients would be associated with a difference in survival.

**2. Methods and materials**

Patient data was obtained from the National Cancer Data Base (NCDB), a joint program of the Commission on Cancer and the American Cancer Society, which includes data from approximately 1500 hospitals and clinics in the United States and its territories. This database captures nearly 70% of new cancer diagnoses made in the United States [28]. All NCDB data is de-identified and therefore exempt from review by our institutional review board.

The initial query included all endometrial cancer patients diagnosed between the years of 2004 and 2013, which yielded 349,404 patients, see Supplementary Fig. 1. Patients were excluded if they lacked indications for adjuvant radiotherapy with curative intention. This included FIGO IA, grade 1 or 2, FIGO stage IVB, or unknown stage (188,172). We further excluded cases with histology other than adenocarcinoma or unknown histology (63,232), and unknown grade (32,472) We excluded cases lacking information on receipt of radiotherapy (1298), or if the radiotherapy was not given adjuvantly (948), not directed at the pelvis (4157), or given to palliative or unrealistic doses (less than 18 or greater than 79 Gray) (109). We excluded cases where chemotherapy receipt was unknown or not given adjuvantly (2187). We excluded cases whose surgical status was unknown or no surgery was performed (583). We excluded cases where no treatment was given, and those with unknown treatment status and survival time (7355).

The primary outcome of interest was receipt of adjuvant radiotherapy, and we sought to understand the impact of age, as well as other clinical and demographic factors, on receipt of adjuvant radiotherapy for

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