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Trends in the utilization of adjuvant chemotherapy in early stage endometrial cancer: a SEER-Medicare study

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Summary

Purpose of Investigation: To examine the utilization of adjuvant chemotherapy in treatment of patients with early stage endometrial cancer in the United States. *Materials and Methods:* The Surveillance, Epidemiology, and End Results (SEER)-Medicare database was used to identify women 65 years or older diagnosed with Stage I/II endometrial cancer from 1991 through 2007. *Results:* A total of 12,885 women met the eligibility criteria. Adjuvant chemotherapy was administered in 2.7% of the patients. In multivariable analysis of predictors of chemotherapy, age ≤ 80 years, residence in northeast region of the United States, diagnosis between years 2003-2007, high tumor grade, non-endometrioid histology, and higher stage disease showed a significant positive association ($p < 0.05$). The usage of chemotherapy increased from 1.5% between years 1991-1994 to 4.2% between years 2003-2007. *Conclusion:* This population-based study shows an increasing trend in the usage of adjuvant chemotherapy for treatment of women with early stage endometrial cancer.

Key words: Trends; Chemotherapy; Early-stage endometrial cancer

Introduction

Endometrial cancer is the most common gynecologic malignancy in the United States. It is estimated that there will be approximately 55,000 new cases and 10,000 deaths due to endometrial cancer in 2015 [1]. Most cases are diagnosed in early stages (Stages I/II) when the disease is still confined to the uterus [2]. Early stage endometrial cancer is associated with excellent prognosis; however a significant heterogeneity exists within this cohort. A high risk population can be identified based on the presence of certain intrauterine factors, which is at increased risk for distant recurrence, and may benefit from administration of adjuvant chemotherapy [3].

Multiple trials have evaluated the role of chemotherapy in early stage endometrial cancer with mixed results. In a combined analysis of two randomized controlled trials, progression-free survival as well as cancer-specific survival was significantly improved with the administration of adjuvant sequential chemotherapy/radiation [4]. A Japanese gynecologic oncology group study randomized patients with deeply invasive Stage I-IIIC endometrial cancer to chemotherapy *vs*. pelvic radiation [5]. Chemotherapy was associated with significantly improved progression-free survival and overall survival in a select high to intermediate risk group defined as [1] patients with myometrial invasion greater than or equal to 50% over 70-years-old or with grade 3 endometrioid adenocarcinoma or [2] patients with Stage II disease or positive peritoneal cytology. The initial results of Gynecologic Oncology Group study (GOG249), which compared external beam radiation to three cycles of chemotherapy with carboplatin and taxol plus vaginal brachytherapy in patients with high-intermediate risk and high-risk endometrial cancer, showed comparable progression-free survival and overall survival between groups, with no superiority of chemotherapy [6]. Similar results have been reported in other randomized controlled trials including patients with early stage endometrial cancer [7].

Given this background, the objective of the current study was to examine the utilization of adjuvant chemotherapy in treatment of patients with early stage endometrial cancer in the United States. To accomplish this goal, the authors used a large cohort derived from the Surveillance, Epidemiology, and End Results (SEER)-Medicare database of the National Cancer Institute.

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Materials and Methods

Study cohort: SEER is a population-based cancer registry that collects information about patient demographics, tumor characteristics, first course of treatment, and survival for persons newly diagnosed with cancer. For people who are Medicare eligible, the Medicare database includes claims for covered healthcare services, including hospital, physician, and outpatient bills [8]. The linkage of persons in the SEER data to their Medicare claims is performed by the National Cancer Institute (NCI) and the Centers for Medicare and Medicaid Services (CMS).

The eligible patients for this study were diagnosed at the age of 65 years and older with primary uterine cancer between January 1, 1991 and December 31, 2007. Only patients diagnosed with FIGO Stage I and II endometrial cancer who underwent a cancer-directed surgery (hysterectomy) were included in the analysis. The authors excluded patients who were members of a Health Maintenance Organization at any point in the 12-month period before and after their cancer diagnosis, those enrolled in Medicare because of end-stage renal disease and dialysis, and patients with other primary tumors. This study was exempted from review by the Institutional Review Board of Wayne State University School of Medicine.

Data extraction: Age at diagnosis was classified into five-year intervals. Stage was assigned from the recorded extent-of-disease codes according to the revised 2009 FIGO staging criteria for endometrial cancer. Surgical procedure data were derived from site-specific surgery codes. Data concerning the performance of lymph node dissection and lymph node metastasis were derived from pathology codes. Information on use of adjuvant external beam radiation therapy (EBRT) and vaginal brachytherapy (VBT) was collected. Medicare claims files [physician (NCH), outpatient (OUTPAT), and hospital (MEDPAR)] were used to identify receipt of chemotherapy within six months of cancer diagnosis. Socioeconomic status and education level of each patient was evaluated respectively by describing the median annual household income and the percentage of population with high school education within the census tract in which the patient resided at the time of diagnosis. The study cohort was divided into approximate tertiles individually according to the median annual household income and the education level for purposes of analysis. The authors included a modified version of the Charlson comorbidity index, which was based on the ICD-9 diagnostic and procedure codes as well as on the Healthcare Common Procedure Coding System (HCPS) codes for ten conditions, captured in the 12-month period before cancer diagnosis [9, 10]. Comorbidity index was categorized into none, one, and two or more. Area of residence was categorized as urban or rural, and the registry in which each patient was recorded was noted.

Statistical analyses: The distribution of demographic and clinical characteristics within the patient cohort was compared by using chi-square tests. The trends of chemotherapy usage over time were examined using chi-square tests. Multivariable logistic regression models were developed to examine the predictors of chemotherapy. SPSS Statistics version 19 was used for all statistical analyses. All *p*-values reported are two-tailed, and a *p*-value of less than 0.05 was considered to be statistically significant.

Results

A total of 12,885 women met the eligibility criteria (Table 1). The mean age of the patients was 75 years (range: 66-101). The majority of the patients were white and resided in urban areas. The geographic distributions of the patients were as follows: 20.5% from the northeast, 22.8% from the

Table 1. — *Clinical and demographic characteristics of women 65 years and older diagnosed with Stage I/II endometrial cancer.*

	n. (12,885)	%
Age (years)		
65-69	3,247	25.2
70-74	3,816	29.6
75-79	3,093	24.0
80-84	1,808	14.0
≥ 85	921	7.2
Race		
White	11,856	92.0
Black	508	4.0
Other/missing	521	4.0
Year of diagnosis		
1991-1994	2,416	18.8
1995-1998	2,357	18.3
1999-2002	3,367	26.1
2003-2007	4,745	36.8
Marital status		
Unmarried	6,486	50.4
Married	5,997	46.5
Unknown	402	3.1
Area of residence		
Rural	1,266	9.8
Urban	11,619	90.2
SEER registry		
Northeast	2,639	20.5
Midwest	2,936	22.8
South	1,359	10.5
West	5,951	46.2
Median household income[1]		
First (lowest) tertile	5,111	39.7
Second tertile	4,490	34.8
Third (highest) tertile	3,284	25.5
High-school education[2]		
First (lowest) tertile	4,281	33.2
Second tertile	4,187	32.5
Third (highest) tertile	4,417	34.3
Comorbidity score		
0	9,207	71.5
1	2,557	19.8
> 2	1,121	8.7
Histology		
Endometrioid	7,468	58.0
Adenocarcinoma not otherwise specified	4,556	35.4
Mucinous	196	1.5
Clear cell	168	1.3
Serous	497	3.8
Grade		
1	5,232	40.6
2	4,595	35.7
3	2,243	17.4
Unknown	815	6.3
Stage		
IA	9,050	70.2
IB	2,796	21.7
II	1,039	8.1
Lymphadenectomy		
No	6,749	52.4
Yes	6,112	47.4
Unknown	24	0.2
External beam radiation		
No	10,401	80.7
Yes	2,484	19.3
Vaginal brachytherapy		
No	11,290	87.6
Yes	1,595	12.4
Chemotherapy		
No	12,537	97.3
Yes	348	2.7

[1]Median household income level within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: < $40,000; second tertile: $40,000-$60,000; third (highest) tertile: > $60,000]

[2]Percentage of population with high-school education within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: 0 - 21.8%; second tertile: 21.8% - 31.4%; third (highest) tertile: 31.4% - 55.8%]

Table 2. — *Clinical and demographic characteristics by receipt of adjuvant chemotherapy among patients with Stage I/II endometrial cancer.*

	Chemotherapy		*p* value
	n. (n=12537)	Yes (n=348)	
Age (years)			< 0.001
65-69	3,122 (96.2%)	125 (3.8%)	
70-74	3,707 (97.1%)	109 (2.9%)	
75-79	3,020 (97.6%)	73 (2.4%)	
80-84	1,782 (98.6%)	26 (1.4%)	
≥ 85	906 (98.4%)	15 (1.6%)	
Race			< 0.001
White	11,553 (97.4%)	303 (2.6%)	
Black	478 (94.1%)	30 (5.9%)	
Other	479 (97.0%)	15 (3.0%)	
Year of diagnosis			< 0.001
1991-1994	2,380 (98.5%)	36 (1.5%)	
1995-1998	2,315 (98.2%)	42 (1.8%)	
1999-2002	3,298 (98.0%)	69 (2.0%)	
2003-2007	4,544 (95.8%)	201 (4.2%)	
Marital status			0.88
Unmarried	6,310 (97.3%)	176 (2.7%)	
Married	5,837 (97.3%)	160 (2.7%)	
Area of residence			0.04
Rural	1,243 (98.2%)	23 (1.8%)	
Urban	11,294 (97.2%)	325 (2.8%)	
SEER registry			< 0.001
Northeast	2,503 (94.8%)	136 (5.2%)	
Midwest	2,872 (97.8%)	64 (2.2%)	
South	1,325 (97.5%)	34 (2.5%)	
West	5,837 (98.1%)	114 (1.9%)	
Median household income[1]		0.008	
First (lowest) tertile	4,997 (97.8%)	114 (2.2%)	
Second tertile	4,366 (97.2%)	124 (2.8%)	
Third (highest) tertile	3,174 (96.7%)	110 (3.3%)	
High-school education[2]			0.04
First (lowest) tertile	4,187 (97.8%)	94 (2.2%)	
Second tertile	4,063 (97.0%)	124 (3.0%)	
Third (highest) tertile	4,287 (97.1 %)	130 (2.9%)	
Comorbidity score			0.02
0	8,975 (97.5%)	232 (2.5%)	
1	2,468 (96.5%)	89 (3.5%)	
> 2	1,094 (97.6%)	27 (2.4%)	
Histology			<0.001
Endometrioid	7,330 (98.2%)	138 (1.8%)	
Adenocarcinoma not otherwise specified/mucinous	4,689 (98.7%)	63 (1.3%)	
Clear cell	146 (86.9%)	22 (13.1%)	
Serous	372 (74.8%)	125 (25.2%)	
Grade			< 0.001
1	5,187 (99.1%)	45 (0.9%)	
2	4,517 (98.3%)	78 (1.7%)	
3	2,077 (92.6%)	166 (7.4%)	
Stage			< 0.001
IA	8,862 (97.9%)	188 (2.1%)	
IB	2,700 (96.6%)	96 (3.4%)	
II	975 (93.8%)	64 (6.2%)	
Lymphadenectomy			< 0.001
No	6,649 (98.5%)	100 (1.5%)	
Yes	5,865 (96.0%)	247 (4.0%)	
External beam radiation		<0.001	
No	10,159 (97.7%)	242 (2.3%)	
Yes	2,378 (95.7%)	106 (4.3%)	
Vaginal brachytherapy		<0.001	
No	11,031 (97.7%)	259 (2.3%)	
Yes	1,506 (94.4%)	89 (5.6%)	

[1]Median household income level within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: < $40,000; second tertile: $40,000 - $60,000; third (highest) tertile: > $60,000]
[2]Percentage of population with high-school education within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: 0 - 21.8%; second tertile: 21.8% - 31.4%; third (highest) tertile: 31.4% - 55.8%]

Table 3. — *Multivariable logistic regression models to determine predictors of receipt of adjuvant chemotherapy in treatment of patients with Stage I/II endometrial cancer.*

	Chemotherapy
Age (years)	OR (95%CI)
65-69	Referent
70-74	*0.67 (0.49-0.93)
75-79	*0.55 (0.38-0.78)
80-84	*0.28 (0.17-0.46)
≥ 85	*0.33 (0.18-0.62)
Race	
White	Referent
Black	1.09 (0.65-1.83)
Other	1.50 (0.83-2.74)
Year of diagnosis	
1991-1994	Referent
1995-1998	0.76 (0.45-1.28)
1999-2002	1.01 (0.63-1.62)
2003-2007	*1.74 (1.11-2.75)
Marital status	
Unmarried	Referent
Married	0.82 (0.63-1.07)
Area of residence	
Rural	Referent
Urban	1.02 (0.59-1.77)
SEER registry	
Northeast	Referent
Midwest	*0.44 (0.29-0.67)
South	*0.48 (0.29-0.77)
West	*0.42 (0.29-0.60)
Median household income[1]	
First (lowest) tertile	Referent
Second tertile	1.21 (0.86-1.70)
Third (highest) tertile	1.32 (0.87-2.01)
High-school education[2]	
First (lowest) tertile	Referent
Second tertile	1.02 (0.72-1.45)
Third (highest) tertile	0.99 (0.65-1.49)
Comorbidity score	
0	Referent
1	1.27 (0.94-1.73)
>2	0.75 (0.46-1.22)
Histology	
Endometrioid	Referent
Adenocarcinoma not otherwise specified	1.20 (0.84-1.72)
Clear cell	*4.41 (2.28-8.54)
Mucinous	0.50 (0.07-3.67)
Serous	*12.09 (8.37-17.45)
Grade	
1	Referent
2	*1.64 (1.11-2.43)
3	*3.92 (2.62-5.86)
Stage	
IA	Referent
IB	*1.79 (1.30-2.46)
II	*2.25 (1.52-3.32)
Lymphadenectomy	
No	Referent
Yes	1.29 (0.96-1.73)
External beam radiation	
No	Referent
Yes	0.90 (0.66-1.23)
Vaginal brachytherapy	
No	Referent
Yes	1.24 (0.89-1.73)

*p value < 0.05
[1]Median household income level within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: < $40,000; Second tertile: $40,000 - $60,000; third (highest) tertile: > $60,000]
[2]Percentage of population with high-school education within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: 0 - 21.8%; second tertile: 21.8% - 31.4%; third (highest) tertile: 31.4% - 55.8%]

Table 4. — *Time trends in utilization of adjuvant chemotherapy in treatment of patients with Stage I/II endometrial cancer.*

	1991-1994	1995-1998	1999-2002	2003-2007	*p* value
Age (years)					
65-69	2.3%	2.9%	2.2%	5.9%	< 0.001
70-74	1.4%	1.7%	3.0%	4.3%	< 0.001
75-79	1.3%	1.1%	1.7%	4.2%	< 0.001
80-84	0.4%	1.8%	0.9%	2.1%	0.14
≥ 85	1.4%	0.8%	1.2%	2.3%	0.57
Race					
White	1.5%	1.8%	1.9%	3.9%	< 0.001
Black	0%	3.0%	3.7%	9.1%	0.02
Other	1.5%	1.1%	2.8%	4.7%	0.32
Marital status					
Unmarried	1.5%	1.9%	1.9%	4.3%	< 0.001
Married	1.5%	1.5%	2.2%	4.1%	< 0.001
Area of residence					
Rural	1.0%	0.4%	1.1%	3.8%	0.002
Urban	1.5%	2.0%	2.2%	4.3%	< 0.001
SEER registry					
Northeast	2.5%	7.0%	3.8%	6.3%	0.004
Midwest	1.4%	1.1%	2.4%	3.8%	0.001
South	0.8%	0.8%	2.1%	3.4%	0.15
West	1.3%	1.1%	1.1%	3.4%	< 0.001
Median household income[1]					
First (lowest) tertile	1.1%	1.2%	1.6%	4.4%	< 0.001
Second tertile	2.3%	1.7%	2.2%	3.8%	0.006
Third (highest) tertile	1.3%	2.8%	2.4%	4.6%	0.004
High-school education[2]					
First (lowest) tertile	1.2%	1.7%	1.4%	3.6%	< 0.001
Second tertile	1.9%	1.9%	2.5%	4.3%	0.001
Third (highest) tertile	1.3%	1.8%	2.3%	4.9%	< 0.001
Comorbidity score					
0	1.4%	1.7%	1.8%	4.3%	< 0.001
1	2.3%	1.7%	2.7%	5.0%	0.003
> 2	1.4%	2.4%	2.9%	2.4%	0.83
Histology					
Endometrioid	1.6%	1.5%	1.1%	2.5%	0.001
Adenocarcinoma not otherwise specified	1.3%	0.8%	1.5%	2.1%	0.12
Mucinous	2.3%	2.1%	0%	0%	0.50
Clear cell	0%	2.7%	10.5%	28.3%	< 0.001
Serous	7.0%	15.8%	21.4%	36.6%	< 0.001
Grade					
1	1.1%	0.8%	0.7%	0.9%	0.84
2	0.8%	0.8%	1.7%	2.8%	< 0.001
3	3.8%	4.0%	5.2%	12.5%	< 0.001
Stage					
IA	1.2%	1.8%	1.8%	2.9%	0.001
IB	1.7%	0.7%	1.7%	6.2%	< 0.001
II	2.9%	3.4%	6.1%	10.5%	< 0.001
Lymphadenectomy					
No	1.1%	1.3%	1.4%	2.0%	0.11
Yes	2.4%	2.6%	2.8%	5.6%	< 0.001
External beam radiation					
No	1.2%	1.8%	1.8%	3.5%	< 0.001
Yes	2.4%	1.8%	3.3%	8.2%	< 0.001
Vaginal brachytherapy					
No	1.2%	1.5%	1.8%	3.6%	< 0.001
Yes	3.7%	4.2%	3.9%	8.1%	0.005

[1]Median household income level within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: < $40,000; second tertile: $40,000 - $60,000; third (highest) tertile: > $60,000]

[2]Percentage of population with high-school education within the census tract in which the patient resided at the time of diagnosis [first (lowest) tertile: 0 - 21.8%; second tertile: 21.8% - 31.4%; third (highest) tertile: 31.4% - 55.8%]

midwest, 10.5% from the south, and 46.2% from the west. Over one quarter of patients (28.5%) had co-morbidities as determined by a modified Charlson co-morbidity index score equal to or greater than one. Endometrioid adenocarcinoma represented the dominant histologic sub-type (58%). Clear cell adenocarcinoma and serous carcinoma were both rare, accounting for 1.3% and 3.8% of the study cohort, respectively. Based on tumor grade, 40.6% tumors were grade 1, 35.7% were grade 2, and 17.4% were grade 3. The majority of the patients had Stage IA disease

(70.2%). Stage IB and II disease were less common, accounting for 21.7% and 8.1% of the study cohort, respectively. Lymphadenectomy was performed in 47.4% of the patients. Adjuvant EBRT was administered in 19.3% of the patients. VBT was given in 12.4% patients. Only 2.7% of the patients received adjuvant chemotherapy.

The demographic and clinical characteristics of the patients were compared according to receipt of chemotherapy as shown in Table 2. Younger patients (age < 80 years), African-American patients, patients diagnosed in 2003-2007, patients residing in urban areas, patients residing in the northeastern U.S., patients with co-morbidity score less than two, patients with non-endometrioid histologies, patients with Stage IB or II disease, patients with higher grade tumors, and those who underwent a lymphadenectomy or received adjuvant EBRT or VBT were more likely to receive chemotherapy ($p < 0.05$ for each). Conversely, patients residing in a census tract with lowest percentage of people with high-school education or lowest median household income were less likely to receive adjuvant chemotherapy ($p < 0.05$).

The authors used multivariable logistic regression to determine the predictors of adjuvant chemotherapy (Table 3). Older age and residence not in northeast were negative predictors of receipt of adjuvant chemotherapy ($p < 0.05$). More recent year of diagnosis (2003-2007), clear cell and serous histologies, higher tumor grade, and higher stage were positively associated with receipt of adjuvant chemotherapy ($p < 0.05$).

Table 4 shows trends in the utilization of chemotherapy over the study period according to different demographic and clinico-pathologic characteristics. The use of chemotherapy increased significantly over time in all age categories except for those including patients aged greater than or equal to 80 years. A similar uptrend in the usage of chemotherapy was noted among white as well as black patients. When considering chemotherapy trends by location of SEER registry, a significant increase in chemotherapy usage was noted in northeast, midwest, and the west, but not in the south. Based on co-morbidity score, the use of chemotherapy was noted to have increased significantly among patients with co-morbidity score zero and one, but not among those with co-morbidity score greater than or equal to two.

When considering the trend regarding chemotherapy administration by histologic type (Table 4), an increase in adjuvant chemotherapy use over time was observed for endometrioid type (1.6% in 1991-1994 to 2.5% in 2003-2007, $p = 0.001$), clear cell type (0% in 1991-1994 to 28.3% in 2003-2007, $p < 0.001$), and serous type endometrial cancer (7.0% in 1991-1994 to 36.6% in 2003-2007, $p < 0.001$). There was also a significant increase in chemotherapy administration rates for grade 2 (0.8% in 1991-1994 to 2.8% in 2003-2007, $p < 0.001$) and grade 3 tumors (3.8% in 1991-1994 to 12.5% in 2003-2007, $p < 0.001$) but not for grade 1 tumors (1.1% in 1991-1994 to 0.9% in 2003-2007, $p = 0.84$). When stratified by stage, a significant increase in chemotherapy administration was observed in all stage groups examined; Stage IA (1.2% in 1991-1994 to 2.9% in 2003-2007, $p = 0.001$), Stage IB (1.7% in 1991-1994 to 6.2% in 2003-2007, $p < 0.001$), and Stage II (2.9% in 1991-1994 to 10.5% in 2003-2007, $p < 0.001$).

The impact of lymphadenectomy on usage of chemotherapy over time was examined (Table 4). The chemotherapy administration rates significantly increased among those who underwent a lymphadenectomy, but not in those who did not undergo a lymph node dissection. When examined by use of external beam radiation or vaginal brachytherapy, chemotherapy usage was noted to have increased among patients who received EBRT or VBRT, as well as those who did not receive these treatments.

Discussion

Only a small percentage of patients received adjuvant chemotherapy in the present study. The tumor-related factors significantly co-related with the administration of adjuvant chemotherapy included histology, tumor grade, and disease stage.

The patients with serous and clear cell endometrial cancer were significantly more likely to receive adjuvant chemotherapy compared to those being treated for endometrioid type endometrial cancer. Multiple studies have shown that patients with early stage uterine papillary serous or clear cell cancer have different recurrence patterns with a greater propensity to develop distant recurrences compared to those diagnosed with early stage endometrioid type endometrial cancer [11-14]. Additionally, unlike endometrioid type endometrial cancer where adjuvant radiation is effective, treatment failures have been reported to occur within the radiation fields in serous and clear cell endometrial cancer types [15]. These observations have led to an increasing use of adjuvant chemotherapy in treatment of serous and clear cell endometrial cancers. Improved outcomes have been reported in several retrospective studies among early-stage patients with serous and clear cell endometrial cancer that were treated with chemotherapy compared with those treated with adjuvant radiation or no further treatment [13, 16-18]. In one of the largest series of Stage I/II papillary serous endometrial cancer, a significant improvement was noted in recurrence rates, progression-free survival, and overall survival in patients treated with platinum based regimens [13]. The current National Comprehensive Network Guidelines (NCCN) also recommend adjuvant chemotherapy in treatment of serous and clear cell endometrial cancer patients who are diagnosed with Stage IA (with myometrial invasion), or Stage IB-IV disease [19].

Significantly more patients with higher grade disease received adjuvant chemotherapy compared to those diag-

nosed with grade 1 disease. Similar results were reported in a recent survey of the practice patterns of Society of Gynecologic Oncology members regarding treatment of early stage endometrial cancer [20]. Tumor grade has been shown to be a significant prognostic factor in endometrial cancer in multiple studies [21-23]. In a GOG 33 study, tumor grade 3 was reported to be the greatest determinant of recurrence among patients with clinical Stage I or II endometrial cancer [24]. Additionally, multiple studies have shown comparable survival outcomes between patients with grade 3 endometrioid cancer and those with papillary serous or clear cell endometrial cancer [25, 26]. When analyzing patterns of failure, no significant difference has been reported between grade 3 endometrioid cancer and papillary serous or clear cell endometrial cancer in frequency of recurrence in the abdomen, pelvis or distant sites [27].

As expected the use of chemotherapy among patients with early stage endometrial cancer was significantly correlated with disease stage. Patients with Stage IB and II endometrial cancer were significantly more likely to be treated with adjuvant chemotherapy compared to those diagnosed with Stage IA disease. Deep myometrial invasion and cervical stromal invasion have been shown to be strong risk-factors for hematogeneous, lymphatic, and peritoneal recurrence in different studies [3]. The recognition of the potential for extra-pelvic recurrence likely dictates the incorporation of systemic cytotoxic therapy in treatment of these patients.

The use of adjuvant chemotherapy was significantly lower in elderly patients. The likelihood of receiving chemotherapy sharply declined with advancing age with a significant downtrend noted from age 80 years onward. Multiple studies have shown that elderly patients are less likely to be offered treatments even when the treatments are thought to be curative [28-30]. Often these patients have pre-existing medical co-morbidities [31]. There is also a natural decline of organ function and bone marrow reserve which may negatively influence the provider decision to administer aggressive treatments [32]. Patient preferences may also contribute to treatment decisions.

Interestingly, significant regional variation was found with regards to administration of chemotherapy for patients with early-stage endometrial cancer, which persisted after adjusting for various demographic and clinico-pathologic variables. Patients receiving treatment in the northeast region of the United States were more likely to be treated with chemotherapy compared to those receiving treatment in the south, west or the midwest regions. This finding suggests that location affects the treatment administered to women diagnosed with early-stage endometrial cancer in the United States. Whether it is a reflection of lack of availability of suitable facilities and trained providers in certain regions or reluctance of physicians/patients in these areas to administer/undergo aggressive treatment could not be determined. However, similar observation has been made by other investigators in cancer of other body sites [33, 34].

The usage of chemotherapy was noted to have increased significantly in later years in the current study. Furthermore, this increase was seen in almost all the different categories examined, which suggests a general trend of an overall increase in the administration of chemotherapy for treatment of early stage endometrial cancer between years 2003-2007. Multiple clinical trials that evaluated the role of chemotherapy in endometrial cancer were published around 2006 [7, 35]. The results of GOG122 confirmed the superiority of chemotherapy over radiation in treatment of advanced stage endometrial cancer [35]. This landmark study reshaped the management of endometrial cancer, and firmly established the role of chemotherapy in treatment of endometrial cancer.

The major strength of this population-based study is the examination of treatment patterns at the community-level using a large cohort of patients with early stage endometrial cancer. Several limitations of this study must be acknowledged. First, the authors included only patients at least 65 years of age, so the results may not be generalizable to younger patients. Second, the SEER-Medicare dataset lacks important clinical data regarding some tumor characteristics such as the presence of lymphovascular space invasion. Third, although the use of chemotherapy was recorded, details regarding the chemotherapy cycles and dosing were not available. Similarly, data regarding radiation techniques such as treatment fields, dose, and fractionation were not included. Finally, given that lymph node dissection was not performed in all patients, understaging is possible. There is some suggestion that patients with incomplete surgical staging are more likely to be offered chemotherapy, and may have influenced some of the present results [36].

Conclusion

In summary, only a small percentage of patients with early stage endometrial cancer are treated with adjuvant chemotherapy; however, the proportion of patients treated with chemotherapy has increased over time. A significant regional variation exists with regards to administration of chemotherapy in patients with early stage endometrial cancer in the United States. Chemotherapy is mainly utilized in treatment of younger patients diagnosed with non-endometrioid histologies, high grade tumors, and higher early stage disease.

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