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ORIGINAL REPORT

Influence of Gynecologic Oncologists on the Survival of Patients With Endometrial Cancer

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ABSTRACT

Purpose
Despite a lack of evidence for survival benefit, the American College of Obstetrics and Gynecology has recommendations for referral to gynecologic oncologists for the treatment of endometrial cancer. Therefore, we propose to determine the influence of gynecologic oncologists on the treatment and survival of patients with endometrial cancer.

Patients and Methods
Data were obtained from Medicare and Surveillance, Epidemiology, and End Results (SEER) databases from 1988 to 2005. Kaplan-Meier and Cox proportional hazard methods were used for analyses.

Results
Of 18,338 women, 21.4% received care from gynecologic oncologists (group A) while 78.6% were treated by others (group B). Women in group A were older (age > 71 years: 49.6% *v* 44%; $P < .001$), had more lymph nodes (> 16) removed (22% *v* 17%; $P < .001$), presented with more advanced (stages III to IV) cancers (21.9% *v* 14.6%; $P < .001$), had higher-grade tumors ($P < .001$), and were more likely to receive chemotherapy for advanced disease (22.6% *v* 12.4%; $P < .001$). In those with stages II to IV disease, the 5-year disease-specific survival (DSS) of group A was 79% versus 73% in group B ($P = .001$). Moreover, in advanced-stage (III to IV) disease, group A had 5-year DSS of 72% versus 64% in group B ($P < .001$). However, no association with DSS was identified in stage I cancers. On multivariable analysis, younger age, early stage, lower grade, and treatment by gynecologic oncologists were independent prognostic factors for improved survival.

Conclusion
Patients with endometrial cancer treated by gynecologic oncologists were more likely to undergo staging surgery and receive adjuvant chemotherapy for advanced disease. Care provided by gynecologic oncologists improved the survival of those with high-risk cancers.

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INTRODUCTION

Endometrial cancer is the most common pelvic gynecologic cancer in the United States with an estimated 42,160 new cases in 2009.[1] Over the last 20 years, the number of annual deaths from uterine cancer has doubled. Research is needed to determine the demographic, clinicopathologic, and treatment factors that may be responsible for the current trend and outcome of patients with endometrial cancer.[2]

In ovarian cancer, the centralization of cancer care resulted in more comprehensive staging, cytoreductive surgery, appropriate use of adjuvant therapy, and better survival.[3] Others have also demonstrated that patients with ovarian cancer who received care from a gynecologic oncologist (GO) underwent a more thorough staging surgery and the use of chemotherapy in high-risk disease with improved survival.[4] Although guidelines for referral to GOs have been established, there is limited information on the influence of subspecialists on the survival of patients with endometrial cancer. Prior studies have shown that GOs are more likely to perform staging procedures with lymph node dissections (LNDs); however, the majority of endometrial cancer patients present with low-risk disease with good outcomes. Thus, the potential positive impact of subspecialty care in endometrial cancer may be more difficult to demonstrate. Moreover, the role of LND in early-stage uterine cancer is controversial.[5] In fact, two recent randomized clinical trials[6,7] showed that LND was not associated with an improved survival in patients with endometrial cancer. Furthermore, since only a subset of advanced-stage patients need radical surgery and adjuvant chemotherapy, it remains to be determined whether subspecialty care by GOs can improve the outcomes of patients with endometrial cancer. Therefore, we

propose to investigate the influence of GOs on staging, adjuvant treatment, and survival of patients with endometrial cancer.

PATIENTS AND METHODS

Data were obtained from the Surveillance, Epidemiology and End Results (SEER) Program and the Centers for Medicare and Medicaid Services Medicare Master Enrollment file between 1991 and 2002.[8] Information reported to SEER includes demographic characteristics, date of diagnosis, stage and grade of tumor, treatment, and follow-up information. For each Medicare beneficiary, there are data from the Medicare master enrollment files, Part A and Part B entitlement, and health maintenance organization enrollment status. A unique identifier in the SEER-Medicare file can be linked with National Claims History records. These noninstitutional claims data contain billed services, largely from physicians or providers in the office, hospital, or other sites. Each billed procedure is identified by a common procedure terminology code accompanied with diagnostic codes (International Classification of Diseases, 9th revision, Clinical Modification [ICD-9-CM]). Race/ethnicity was classified into white, black, Hispanic, Asian, and other. Geographic regions were divided into Western, Eastern, and Central states by using state codes based those in the SEER database. By using the median income of the ZIP code of the patient's residence, socioeconomic status was estimated on the basis of the following definition: low (< $20,000/year), intermediate ($20,000-$60,000/year), and high (> $60,000/year) income groups.

Information on primary surgery and the use of chemotherapy was obtained from SEER-Medicare codes. All patients diagnosed with endometrial cancer were staged by using American Joint Committee on Cancer (AJCC) codes, and the histologic cell types were classified as endometrioid, papillary serous, clear-cell, or other and were designated as grade 1, 2, or 3.

The methodology of ascertaining subspecialty care by a GO has been previously described.[9] We extracted information regarding surgeon specialty from the cancer-directed procedures by linking physicians' unique provider identification numbers in Medicare claims to information collected by the American Medical Association. If more than one surgeon was involved in the care of a patient, care was attributed to the most specialized surgeon. For instance, if a GO was ever involved in a patient's care, the patient was categorized as having received care by a GO. In surgeries in which a GO was not involved but a general gynecologist was present, then the patient's care was attributed to a general gynecologist. If neither a GO nor a general gynecologist was involved, the patient was classified as having had surgery performed by a general surgeon.

Overall survival was determined from the time of diagnosis until death or censoring. Disease-specific survival was determined from the time of diagnosis until death from endometrial cancer. Deaths from other or unknown causes were censored at the time of death. Pearson's χ^2 test was used to evaluate associations between factors and risk of death. Survival analyses and predictors of outcome were estimated by using Kaplan-Meier and Cox proportional hazard methods, respectively. Statistical analyses were performed by using SAS version 9.1 (SAS Institute, Cary, NC).

RESULTS

Of 18,338 patients with endometrial cancer, the median age at diagnosis was 70 years (range, 27 to 101 years). The ethnic breakdown for this group was 16,593 (90.5%) white, 930 (5.1%) black,

Table 1. Demographic Characteristics

	Care From Gynecologic Oncologist						
	Total (N = 18,338)		Yes (n = 3,927)		No (n = 14,411)		
Demographic Characteristic	No.	%	No.	%	No.	%	*P*
Age at diagnosis, years*							< .001
≤ 71	10,022	54.7	1,980	19.8	8,042	80.2	
> 71	8,316	45.3	1,947	23.4	6,369	76.6	
Race/ethnicity							< .001
White	16,593	91	3,493	88	13,100	90	
Black	930	5.1	241	6	689	4	
Hispanic	168	0.9	43	1	125	0	
Asian	214	1.2	60	1	154	1	
Other	343	1.9	74	1	269	1	
Unknown	54	0.01	7	0.2	47	0.3	
Socioeconomic factor (income)†							< .001
Low	684	3	172	4	512	3	
Intermediate	6,972	38	1,765	44	5,207	36	
High	4,947	27	1,285	32.7	3,689	25	
Unknown	5,330	29	327	17	5,003	34.7	
Region‡							< .001
Western states	5,388	29.3	1,043	26.5	4,295	29.7	
Central states	4,772	25.9	974	24.8	3,798	26.3	
Eastern states	8,237	44.8	1,910	48.6	6,318	43.9	
Year of diagnosis*							< .001
1991-1994	5,444	29.7	582	10.7	4,862	89.3	
1995-1998	5,110	27.9	1,205	23.6	3,905	76.4	
1999-2002	7,784	42.4	2,140	27.5	5,644	72.5	

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.
*Calculated on the basis of the percent of patients cared for by gynecologic oncologists within age group and time period.
†Socioeconomic status was estimated on the basis of the following definition: low (< $20,000/year), intermediate ($20,000-$60,000/year), and high (> $60,000/year) income groups.
‡Geographic regions were divided into western, eastern, and central states by using state codes on the basis of the SEER database.

214 (1.2%) Asian, 168 (0.9%) Hispanics, and 343 (1.9%) other. The number of patients from Western, Central, and Eastern states was 5,388 (29.3%), 4,772 (25.9%), and 8,237 (44.8%), respectively. We divided the study population into three subsets on the basis of years of diagnosis; 1991 to 1994, 1995 to 1998, and 1999 to 2002. The number of patients with endometrial cancer was 5,444 (29.7%), 5,110 (27.9%), and 7,784 (42.4%), respectively, for those subsets. The proportion of patients treated by a GO increased from 10.7% to 23.6% to 27.5% over the three time periods. The study cohort was then divided into two groups depending on whether the patients had been treated by a GO.

Women treated by a GO were older ($P < .001$) and resided in a higher income region ($P < .001$; Table 1) Those who underwent surgery by a GO were more likely to receive a more extensive lymph node resection ($\geq$ 16 lymph nodes; 22% *v* 17%; $P < .001$), have more aggressive histologic cell types such as serous and clear-cell (11.6% *v* 6.1%; $P < .001$), present with advanced-stage disease (stages III and IV; 21.9% *v* 14.6%; $P < .001$), have received chemotherapy (22.6% *v* 12.4%; $P < .001$), and have received radiation (38.9% *v* 30.7%; $P < .001$; Table 2).

Five-year disease-specific survival (DSS) based on demographic features is presented in Table 3. The 5-year DSS of patients with stages I, II, III, or IV disease were 97%, 89%, 78%, and 55%, respectively ($P < .001$). Patients who underwent primary surgery had an improved survival compared with those who did not (92% *v* 73%; $P < .001$). Patients with grade 1, 2, or 3 tumors had survival rates of 98%, 94%, and 75%, respectively. Patients with endometrioid histology had a survival rate of 94% compared with only 77% in those with clear-cell, serous, or other nonendometrioid histologies (Table 4).

Care provided by GOs was associated with an improved DSS in those with stages II to IV disease (5-year DSS, 79% *v* 73%; $P = .001$; Fig 1). More specifically, patients with stages III and IV disease treated by a GO had a survival of 72% compared with 64% for those treated by others ($P < .001$). Similarly, GO care was associated with improved survival in patients with grade 3 disease (82% *v* 78%; $P = .01$) and high-risk clear-cell and papillary serous histologies (81% *v* 75%; $P < .04$; Table 4). However, there was no association of DSS and GO care identified in overall stage I cancers with and without surgical staging. Furthermore, we performed a subset analysis limited to those patients who underwent surgical staging procedures. After adjusting for the effect of surgical staging on those with stage III disease, we found that GO care was no longer associated with an improvement in survival (84.6% *v* 84.4%; $P = .6$). In another analysis to determine the impact of GO care on overall survival rather than DSS of those with advanced-stage disease, our data showed that GO care was associated with improved overall survival (41.8% *v* 35.4%; $P < .001$).

On multivariate analysis, age at diagnosis as a continuous variable (hazard ratio [HR], 1.04; 95% CI, 1.04 to 1.05; $P < .001$), stages I to II versus stages III to IV (HR, 5.89; 95% CI, 5.16 to 6.72; $P < .001$), grade 1 versus grade 2 versus grade 3 (HR, 2.87; 95% CI, 2.52 to 3.28;

Table 2. Clinicopathologic Characteristics

	Care From Gynecologic Oncologist						
	Total (N = 18,338)		Yes (n = 3,927)		No (n = 14,411)		
Clinicopathologic Characteristic	No.	%	No.	%	No.	%	*P*
Primary surgery							.001
Yes	17,781	97.0	3,771	96.0	14,010	97.2	
No	557	3.0	156	4.0	401	2.8	
Stage*							< .001
IA	1,393	7.6	150	3.8	1,243	8.6	
IB	958	5.2	131	3.3	827	5.7	
IC	11,548	63.0	2,391	60.8	9,157	63.5	
II	1,452	8.0	395	10.1	1,057	7.3	
III	1,298	7.1	423	10.8	875	6.0	
IV	1,689	9.2	437	11.1	1,252	8.6	
Histology							< .001
Endometrioid	15,090	90.3	3,044	85.6	12,046	91.5	
Serous	904	5.4	314	8.8	590	4.5	
Clear-cell	311	1.9	100	2.8	211	1.6	
Other	406	2.4	95	2.7	311	2.4	
Grade							< .001
1	6,544	35.7	1,074	27.4	5,470	38.0	
2	6,328	43.6	1,403	35.7	4,952	34.4	
3	4,161	22.7	1,124	28.6	3,037	21.1	
Unknown	1,278	7.0	326	8.3	952	6.7	
Radiation							< .001
Yes	5,957	32.5	1,529	38.9	4,428	30.7	
No	12,381	67.5	2,398	61.1	9,983	69.3	
Chemotherapy							< .001
Yes	2,657	14.5	886	22.6	1,791	12.4	
No	15,661	85.5	3,041	77.4	12,620	87.5	

*Patients were staged by using American Joint Committee on Cancer codes.

Table 3. Five-Year Disease-Specific Survival Based on Demographic Characteristics

Demographic Characteristic	Total (N = 18,338; %)	Care From Gynecologic Oncologist		P
		Yes (n = 3,927; %)	No (n = 14,411; %)	
Age, years				
≤ 71	95 ± 0.2	89 ± 0.7	89 ± 0.4	.78
> 71	91 ± 0.3	91 ± 0.3	95 ± 0.2	< .001
Race/ethnicity				
White	92 ± 0.2	90 ± 1	91 ± 0.4	.02
Hispanic	93 ± 1	92 ± 0.4	94 ± 0.2	.66
Asian	96 ± 0.1	90 ± 0.4	98 ± 0.9	.001
Black	83 ± 1	81 ± 2	83 ± 1	.41
Unknown	75 ± 1	71 ± 1.7	84 ± 6	.34
Other	90 ± 2	91 ± 3	89 ± 1	.7
Socioeconomic factor (income)*				
Low	89 ± 1	89 ± 2	90 ± 1	.53
Intermediate	92 ± 0.4	91 ± 0.7	93 ± 0.3	.01
High	92 ± 0.4	92 ± 0.8	93 ± 0.4	.1
Unknown	90 ± 6	90 ± 1	91 ± 8	.002
Region†				
Western states	93 ± 0.2	93 ± 0.4	93 ± 0.8	.97
Central states	91 ± 0.3	91 ± 0.9	92 ± 0.4	.009
Eastern states	91 ± 0.2	90 ± 0.7	92 ± 0.3	.002
Year of diagnosis				
1991-1994	91 ± 0.3	92 ± 0.1	91 ± 0.4	.15
1995-1998	91 ± 0.4	88 ± 0.9	92 ± 0.4	< .001
1999-2002	93 ± 0.2	93 ± 0.6	94 ± 0.3	.28

Abbreviation: SEER, Surveillance, Epidemiology, and End Results.
*Socioeconomic status was estimated on the basis of the following definition: low (< $20,000/year), intermediate ($20,000-$60,000/year), and high (> $60,000/year) income groups.
†Geographic regions were divided into western, eastern, and central states by using state codes on the basis of the SEER database.

$P < .001$), and care by a GO versus no GO (HR, 0.71; 95% CI, 0.62 to 0.82; $P = .001$) were independent prognostic factors for improved survival (Table 5).

DISCUSSION

The number of deaths per year from endometrial cancer has increased in the last decade. A prior study[2] showed that higher stage and poor histologic cell types over time may partially explain the increase in number of the deaths associated with endometrial cancer. However, the impact of specialized care from a GO on the treatment and outcome of endometrial cancer has not been well studied. Previous investigations have assessed the impact of GOs on primary surgery, staging, and use of chemotherapy in other gynecologic malignancies. Vernooij et al[10] performed a meta-analysis showing that care provided by a GO improved the survival of patients with ovarian cancer by up to 8 months. The authors recommended that patients with advanced ovarian cancers should be treated in specialized gynecologic oncology care units by a multidisciplinary team. A study by Carney et al[11] also evaluated subspecialty care on patients with ovarian cancer in the United States and showed that care provided by a GO was associated with a survival benefit. In a large population-based study of patients with ovarian cancer in Northern California, Chan et al[4] demonstrated that GOs were more likely to perform comprehensive staging surgeries and administer adjuvant chemotherapy when appropriate. However, these prior studies have addressed primarily patients with ovarian cancer, and to the best of our knowledge, this study is the first large, population-based study to evaluate the influence of subspecialty care on patients with endometrial cancer.

The results of this analysis showed that patients cared for by GOs typically have more advanced-stage and high-risk (grade 3 and poor histologic type) cancers. Although our univariate analyses showed that older, white, and Asian patients did better without GO care, these findings were confounded by the fact that older women are more likely to receive care by a GO and they had more aggressive cancers with advanced-stage, high-risk histologies and high-grade disease. In another subset analysis of only older (age > 71 years) patients, our data showed that those treated by GOs had more advanced (stages III to IV) disease (24.4% *v* 18.1%; $P < .001$) and high-grade disease (33.5% *v* 25.6%; $P < .001$) compared with those treated by others. More importantly, after adjusting for age, stage, and grade of disease, GO care remained as an independent prognostic factor for improved DSS on multivariate analysis.

Patients cared for by GOs are more likely to undergo staging procedures with lymph node assessment and to receive chemotherapy. The DSS of those with stages II to IV disease who underwent care by GOs had significantly improved survival. These effects persisted in multivariate analysis after adjusting for age, surgery, stage, grade, and histology. The survival benefit associated with care by a GO may be explained by their better understanding of the disease process resulting in more accurate staging followed by adjuvant treatment if indicated.

Table 4. Five-Year Disease-Specific Survival Based on Clinicopathologic Characteristics

Clinicopathologic Characteristic	Total (N = 18,338; %)	Care From Gynecologic Oncologist		P
		Yes (n = 3,927; %)	No (n = 14,411; %)	
Primary surgery				
Yes	92 ± 0.2	91 ± 0.4	93 ± 0.2	.001
No	73 ± 0.2	79 ± 0.4	70 ± 0.2	.10
Primary surgery (stages II to IV)				
Yes	76 ± 0.7	80 ± 0.1	74 ± 0.9	< .001
No	53 ± 0.4	58 ± 0.9	50 ± 0.4	.22
Stage*				
IA	97 ± 0.1	96 ± 1	96 ± 0.5	.2
IB	95 ± 0.7	94 ± 2	95 ± 0.7	.054
IC	97 ± 0.9	96 ± 0.4	97 ± 0.1	.008
II	89 ± 0.8	90 ± 1	89 ± 1	.68
III	78 ± 1	81 ± 2	77 ± 1	.19
IV	55 ± 1	63 ± 2	52 ± 1	< .001
II to IV	75 ± 0.7	79 ± 1	73 ± 0.8	.001
III to IV	66 ± 0.1	72 ± 1	64 ± 1	< .001
Histology				
Endometrioid	94 ± 0.2	92 ± 0.5	94 ± 0.2	.001
Serous, clear-cell, other	77 ± 0.1	81 ± 1	75 ± 1	.04
Grade				
1	98 ± 0.1	97 ± 0.4	98 ± 0.1	< .001
2	94 ± 0.3	93 ± 0.7	94 ± 0.3	.02
3	75 ± 1	82 ± 0.1	78 ± 0.8	.01
Unknown	86 ± 0.1	87 ± 1	85 ± 1	.32
Radiation				
Yes	88 ± 0.1	88 ± 0.1	88 ± 0.1	.41
No	94 ± 0.5	92 ± 0.7	94 ± 0.5	.74
Chemotherapy				
Yes	76 ± 0.9	77 ± 1	76 ± 1	.82
No	94 ± 0.1	95 ± 4	94 ± 0.2	.72

*Patients were staged by using American Joint Committee on Cancer codes.

In addition, we performed a subset analysis limited to those patients who underwent surgical staging procedures. After adjusting for the effect of surgical staging in those with stage III disease, we found that GO care was no longer associated with an improvement in survival (84.6% *v* 84.4%; $P = .6$). The results of this subset analysis suggest that the effect of GO care may be partially attributed to the comprehensive staging procedures and subsequent guidance to appropriate adjuvant therapy for improving survival. Other studies[4,5,12] have also shown that comprehensive surgical staging directs the use of adjuvant treatment and improves survival. Furthermore, the use of comprehensive staging including LND has been shown to improve the detection of patients with node-positive disease in two prospective clinical trials.[6,7] In one of these prospective randomized trials, Benedetti Panici et al[7] showed that 13% of the patients who underwent systematic lymphadenectomy had adjuvant therapy compared with only 3% in those who had lymphadenectomy on the basis of clinical suspicion only.[6,7] However, lymphadenectomy in endometrial cancer has not been shown to improve survival in the overall study group. This may be explained by the fact that most patients with endometrial cancer have early-stage, low-grade disease with an excellent prognosis. Thus, it is difficult to demonstrate the survival benefit associated with LND or subspecialty care in cancers with a relatively favorable prognosis.

Similarly, our results did not show a survival benefit associated with GO care in those with stage I and grade 1 cancers. The overall survival of this group was excellent with a 5-year DSS of 95.0%. It is likely that, given the good prognosis associated with stage I grade 1 disease, we were unable to demonstrate a survival advantage associated with GO care, even in this large cohort of patients with stage I cancers. Likewise, in a recent study of 5,556 low-risk (stage IA, all grades; stage IB, grades 1 and 2) patients, we were unable to show a survival advantage associated with comprehensive surgical staging with lymphadenectomy.[13] However, subspecialty care improved the survival of those with stages II to IV disease, high-grade tumors, and aggressive histologic cell types.

In those with stages III and IV disease, the benefit of GO care may be associated not only with comprehensive surgical staging but also with cytoreduction of metastatic disease. Several studies have demonstrated a benefit of cytoreduction in uterine cancer. Chi et al[14] showed that the extent of cytoreduction had prognostic significance on the survival of patients with stage IV endometrial cancer. In this study of 1,689 stage IV patients, our data showed that care by a GO improved their survival from 52% to 63%, suggesting that cytoreductive surgery may play a role in the survival advantage from GO care.

The impact of GO care on overall survival in addition to DSS was investigated in those with advanced-stage disease. This analysis demonstrated that GO care was associated with improved overall survival (41.8% *v* 35.4%; $P < .001$). It is possible that the effect of GO care is

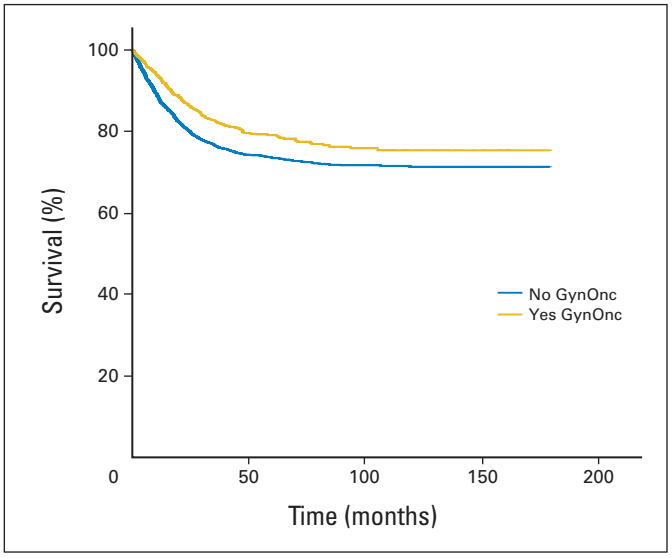

Fig 1. Disease-specific survival of stages II to IV patients on the basis of gynecologic oncologist care (GynOnc; n = 4,439; $P = .001$).

associated not only with better endometrial cancer care including more comprehensive surgical staging and cytoreduction but also with appropriate screening and early detection of other malignancies. In fact, McBean et al[15] showed that patients with endometrial cancer who were cared for by GOs were more likely to receive mammography and colorectal cancer screening compared with a matched group of women with no history of cancer who received care by other primary care providers.

In this study, 45% of patients with endometrial cancer were older (age > 71 years), but only 23.4% of these patients received care by a GO. Moreover, it is important to note that in the overall study group, only 21.4% of patients received subspecialty care. In addition, women with lower socioeconomic status were less likely to receive care by a GO. Other prior studies[4,16,17] in gynecologic cancer also demonstrated the disparities associated with suboptimal treatment. Clearly, further research is needed to identify the disparities in endometrial cancer treatment and potential barriers to accessing subspecialty care. Nevertheless, on the basis of the results of this analysis, we showed that those with poor histologic cell types, higher grade of disease, and advanced stage may benefit from care by a GO. Although grade of disease and cell type can be analyzed to a certain degree of accuracy before surgery, it is not always possible to identify those with advanced-stage disease with nodal metastases until surgical staging is performed. Until there is an accurate preoperative diagnostic test to identify those with advanced-stage disease, women with endometrial cancer should still seek care by a GO to assess the need for surgical staging and guidance for adjuvant therapy after surgery.

Table 5. Multivariate Analysis of Prognostic Factors for Disease-Specific Survival

Factor	Hazard Ratio	95% CI	*P*
Age at diagnosis*	1.04	1.04 to 1.05	< .001
Stage†	5.89	5.16 to 6.72	< .001
Grade‡	2.87	2.52 to 3.28	< .001
Gynecologic oncologist§	0.71	0.62 to 0.82	.001

*Age as a continuous variable.
†Stage I to II v III to IV.
‡Grade 1 v grade 2 v grade 3.
§No gynecologic oncologist *v* yes gynecologic oncologist.

Our study was limited by a lack of information on the extent of residual disease after cytoreductive surgery for advanced disease, lack of central pathology review, unknown types and cycles of adjuvant chemotherapy, and unspecified treatment for recurrent disease. Without central pathology review, it is possible that a change in grade of disease may affect the results of this study. For example, the investigators from the Postoperative Radiation Therapy in Endometrial Carcinoma (PORTEC) trial[18] performed central pathology review and found a substantial shift from grade 2 to grade 1 disease but no significant difference for grade 3 disease. However, despite this shift, the results of their study remained essentially unchanged. Furthermore, it is possible that there may not be unanimous agreement, even after expert pathology review. For instance, gynecologic pathologists who used the International Society of Gynecologic Pathologists/WHO criteria from the Gynecologic Oncology Group performed a central pathology review in preinvasive endometrial disease and found unanimous agreement in only 40% of cases.[19] With respect to the accuracy of pathology, prior studies[20,21] have performed reviews of slides from cancer registries and showed excellent agreement between registry and referral pathologists.

The strengths of our study lie in the large number of patients with endometrial cancer. To our knowledge, this is the first population-based study to analyze the impact of GO care on endometrial cancer patients. The extensive geographic distribution of patients expanding to twelve US regions minimizes the potential surveillance and selection biases that limit other smaller, single-institution studies. Moreover, the results from this population-based study[22] can be generalized to the entire US population since the SEER cancer registries are consistent in representative regions throughout the country. Furthermore, the SEER database is accurate for completeness of each sample case and the use of adjuvant therapy and surgical procedures.[23,24] Prior studies that used smaller institutional databases have reported findings similar to the current study in terms of patients selected for management by GO, but those studies did not report an improvement in DSS in such patients.[25,26]

Our study showed that gynecologic oncologists are more likely than other care providers to treat endometrial cancers with more advanced stage, high grade, and poor histologic cell types. Directed care by gynecologic oncologists was associated with more extensive lymph node resection and subsequent adjuvant therapy. Most importantly, care provided by gynecologic oncologists improved the survival of those with high-risk (stages II to IV, grade 2 and 3, and high-risk histologies) disease. However, nearly 80% of overall endometrial cancer patients in this national study did not receive care by a gynecologic oncologist. Further studies are warranted to identify the potential barriers to subspecialty care access, particularly in those with poorer prognostic cancers.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: John K. Chan, Daniel S. Kapp, Ruxi Zhang, Kathryn E. Osann, Larry Maxwell, Lee-May Chen
Administrative support: John K. Chan, Alexander E. Sherman, Daniel S. Kapp
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REFERENCES

1. Jemal A, Siegel R, Ward E, et al: Cancer statistics, 2009. CA Cancer J Clin 59:225-249, 2009

2. Ueda SM, Kapp DS, Cheung MK, et al: Trends in demographic and clinical characteristics in women diagnosed with corpus cancer and their potential impact on the increasing number of deaths. Am J Obstet Gynecol 198:218. e1-e6, 2008

3. Bristow RE, Santillan A, Diaz-Montes TP, et al: Centralization of care for patients with advanced-stage ovarian cancer: A cost-effectiveness analysis. Cancer 109:1513-1522, 2007

4. Chan JK, Kapp DS, Shin JY, et al: Influence of the gynecologic oncologist on the survival of ovarian cancer patients. Obstet Gynecol 109:1342-1350, 2007

5. Chan JK, Kapp DS: Role of complete lymphadenectomy in endometrioid uterine cancer. Lancet Oncol 8:831-841, 2007

6. ASTEC study group, Kitchener H, Swart AM, et al: Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): A randomised study. Lancet 373:125-136, 2009

7. Benedetti Panici P, Basile S, Maneschi F, et al: Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: Randomized clinical trial. J Natl Cancer Inst 100:1707-1716, 2008

8. National Cancer Institute: Health Services and Economics: SEER-Medicare Linked Database. www.healthservices.cancer.gov/seermedicare/

9. Earle CC, Schrag D, Neville BA, et al: Effect of surgeon specialty on processes of care and outcomes for ovarian cancer patients. J Natl Cancer Inst 98:172-180, 2006

10. Vernooij F, Heintz P, Witteveen E, et al: The outcomes of ovarian cancer treatment are better when provided by gynecologic oncologists and in specialized hospitals: A systematic review. Gynecol Oncol 105:801-812, 2007

11. Carney ME, Lancaster JM, Ford C, et al: A population-based study of patterns of care for ovarian cancer: Who is seen by a gynecologic oncologist and who is not? Gynecol Oncol 84:36-42, 2002

12. Parthasarathy A, Kapp DS, Cheung MK, et al: Adjuvant radiotherapy in incompletely staged IC and II endometrioid uterine cancer. Obstet Gynecol 110: 1237-1243, 2007

13. Chan JK, Cheung MK, Huh WK, et al: Therapeutic role of lymph node resection in endometrioid corpus cancer: A study of 12,333 patients. Cancer 107:1823-1830, 2006

14. Chi DS, Welshinger M, Venkatraman ES, et al: The role of surgical cytoreduction in Stage IV endometrial carcinoma. Gynecol Oncol 67:56-60, 1997

15. McBean AM, Yu X, Virnig BA: The use of preventive health services among elderly uterine cancer survivors. Am J Obstet Gynecol 198:86.e1-e8, 2008

16. Chan JK, Zhang M, Hu JM, et al: Racial disparities in surgical treatment and survival of epithelial ovarian cancer in United States. J Surg Oncol 97:103-107, 2008

17. Cress RD, O'Malley CD, Leiserowitz GS, et al: Patterns of chemotherapy use for women with ovarian cancer: A population-based study. J Clin Oncol 21:1530-1535, 2003

18. Scholten AN, van Putten WL, Beerman H, et al: Postoperative radiotherapy for Stage 1 endometrial carcinoma: Long-term outcome of the randomized PORTEC trial with central pathology review. Int J Radiat Oncol Biol Phys 63:834-838, 2005

19. Zaino RJ, Kauderer J, Trimble CL, et al: Reproducibility of the diagnosis of atypical endometrial hyperplasia: A Gynecologic Oncology Group study. Cancer 106:804-811, 2006

20. Piver MS, Tsukada Y, Werness BA, et al: Comparative study of ovarian cancer histopathology by registry pathologists and referral pathologists: A study by the Gilda Radner Familial Ovarian Cancer Registry. Gynecol Oncol 78:166-170, 2000

21. Tyler CW Jr, Lee NC, Robboy SJ, et al: The diagnosis of ovarian cancer by pathologists: How often do diagnoses by contributing pathologists agree with a panel of gynecologic pathologists? Am J Obstet Gynecol 164:65-70, 1991

22. Hankey BF, Ries LA, Edwards BK: The surveillance, epidemiology, and end results program: A national resource. Cancer Epidemiol Biomarkers Prev 8:1117-1121, 1999

23. Virnig BA, Warren JL, Cooper GS, et al: Studying radiation therapy using SEER-Medicare-linked data. Med Care 40:IV-49-54, 2002

24. Cooper GS, Virnig B, Klabunde CN, et al: Use of SEER-Medicare data for measuring cancer surgery. Med Care 40:IV-43-8, 2002

25. Roland PY, Kelly FJ, Kulwicki CY, et al: The benefits of a gynecologic oncologist: A pattern of care study for endometrial cancer treatment. Gynecol Oncol 93:125-130, 2004

26. Macdonald OK, Sause WT, Lee RJ, et al: Does oncologic specialization influence outcomes following surgery in early stage adenocarcinoma of the endometrium? Gynecol Oncol 99:730-735, 2005

