Original Article

Site-Specific Factors for Cancer of the Corpus Uteri From SEER Registries: Collaborative Stage Data Collection System, Version 1 and Version 2

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BACKGROUND: Uterine cancer is the fourth leading cancer among US women. Changes in uterine cancer staging were made from the American Joint Committee on Cancer (AJCC) 6th to 7th edition staging manuals, and 8 site-specific factors (SSFs) and 3 histologic schemas were introduced. Carcinomas account for 95% of cases and are the focus of this report. **METHODS:** Distributions of SSF values were examined for 11,601 cases of malignant cancer of the corpus uteri and uterus, NOS (not otherwise specified) diagnosed in Surveillance, Epidemiology, and End Results (SEER) Program registries during 2010. AJCC 6th and 7th edition staging distributions were compared for 11,176 cases using data in both staging systems. AJCC 6th edition staging distributions during 2004-2010 were examined. AJCC 7th edition SSFs required by SEER were International Federation of Gynecology and Obstetrics stage (SSF1), peritoneal cytology (SSF2), number of positive pelvic lymph nodes (SSF3), number of pelvic lymph nodes examined (SSF4), number of positive para-aortic lymph nodes (SSF5), and number of para-aortic lymph nodes examined (SSF6). **RESULTS:** For SSFs related to lymph nodes, a third of cases were classified as "not applicable," reflecting that lymph node dissection is not indicated for cases with stage1A and stage 4 diagnoses. AJCC 7th edition criteria assigned more cases to stage I (72.9%) than AJCC 6th edition criteria (68.7%). Annual counts significantly increased during 2004-2010, as did counts for AJCC 6th edition stages INOS, IA, IB, IC, IIIA, IIIB, IIIC, and IVB. The proportion of cases diagnosed with stage I cancer was stable, whereas stages II and IV decreased and stage III increased. **CONCLUSIONS:** Five SSFs were suitable for analysis: peritoneal cytology results (SSF2), numbers of positive pelvic lymph nodes (SSF3), pelvic lymph nodes examined (SSF4), positive para-aortic lymph nodes (SSF5), and para-aortic lymph nodes examined (SSF6). ***Cancer* 2014;120(23 suppl):3836-45.** © *2014 American Cancer Society.*

KEYWORDS: corpus uteri, cancer staging, SEER, collaborative stage.

INTRODUCTION

Among cancers of the female genital system, corpus uteri and corpus, not otherwise specified (NOS) is the most commonly diagnosed cancer and the second most common cause of cancer death after ovarian cancer. Overall, uterine cancer is the fourth most frequently diagnosed cancer among women in the United States, with 49,560 newly diagnosed cases and 8190 deaths estimated to occur during 2013.[1] Incidence rates historically have been slightly higher among white women than black women and women of other races; however, the mortality rate among black women is almost twice that of other women.[2] Factors affecting racial variation include tumor aggressiveness and racial differences in the prevalence of hysterectomy.[3,4] In recent years, the incidence rate of corpus uteri and corpus, NOS cancer has been increasing among women of all major racial and ethnic groups. Estrogen unopposed by progesterone is a main risk factor for endometrial cancer; and the increasing prevalence of obesity is thought to contribute to the recent increase in incidence.[5] Diabetes and nulliparity are both risk factors that are increasing among US women.[6,7] The majority of cancer cases of the corpus uteri are diagnosed as International Federation of Gynecology and Obstetrics (FIGO) stage I.[8] Among more aggressive histologies, such as clear cell adenocarcinoma and serous cancers, cases often present at a more advanced stage and with worse prognosis. In these instances curative surgery may not be a treatment option.

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Surgical staging of uterine cancers involves removal of the uterus, cervix, ovaries, and fallopian tubes and potentially dissection of the pelvic and para-aortic lymph nodes.[8] Biopsies are performed on areas of suspected metastases. Omentectomy is typically is reserved for more aggressive histologic subtypes. National Comprehensive Cancer Network guidelines for surgical management and use of lymphadenectomy for staging of endometrial cancer give consideration to pre- and intraoperative findings, extent of metastasis, and surgical risk associated with comorbidities.[9] Important prognostic factors of endometrial cancer are stage, grade, and lymph node positivity.[10-12] For surgical staging of gynecologic cancers, many countries follow standards set by FIGO.[13] The 7th edition of the *American Joint Committee on Cancer (AJCC) Staging Manual*, published in January 2010, includes the same staging categories as the FIGO staging guidelines of 2008, except that the AJCC 7th edition does not include IIICNOS or IVNOS. [14] Revisions in uterine cancer staging in the AJCC 7th edition, compared with the AJCC 6th edition, include but are not restricted to reassigning stage IIA cases to various subgroups of stage I and of some stage IIIA cases to stage I and II subgroups. In addition, approximately 15% of unknown stage cases under the AJCC 6th edition were reclassified to specific stages I, II, and II subcategories under the AJCC 7th edition. Like changes in FIGO staging guidelines, AJCC 7th edition revisions were made to improve the prediction of prognosis.[15,16] Additional changes in the AJCC 7th edition include the collection of 8 site-specific factors (SSFs), 6 of which were required by the Surveillance, Epidemiology, and End Results (SEER) Program: FIGO stage (SSF1), peritoneal cytology results (SSF2), number of positive pelvic lymph nodes (SSF3), number of pelvic lymph nodes examined (SSF4), number of positive para-aortic lymph nodes (SSF5), and number of para-aortic lymph nodes examined (SSF6). Collection of data for the other 2 SSFs, percentage of non–endometrioid cell type in mixed histology tumors (SSF7) and omentectomy (SSF8) were deemed optional. Another change was the separation of corpus uteri cancer cases into 3 separate histology-based staging schemas—carcinoma, sarcoma, and adenosarcoma. This report is restricted to the predominant schema, uterine carcinomas. We examined AJCC 6th edition staging trends during 2004-2010, the effect of the changes in staging criteria between the AJCC 6th and 7th editions, and the completeness of SSF data collected in 2010.

MATERIALS AND METHODS

Analytic Cohorts

The SEER November 2012 submission file was used for all analyses. Cases resided in 18 SEER registries covering 28% of the US population (also called the SEER-18): San Francisco (SF)–Oakland standard metropolitan statistical area, Connecticut, Detroit (metropolitan), Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Atlanta (metropolitan), San Jose–Monterey (SJM), Los Angeles, Alaska Natives, rural Georgia, California excluding SF/SJM/Los Angeles, Kentucky, Louisiana, New Jersey, greater Georgia.

TABLE 1. Exclusion Criteria for Corpus Uteri Analyses, SEER, 2010 Cases

Exclusion Criteria	AJCC 6th and 7th Edition Stage Criteria 1	SSFs Criteria 2
In situ cases	Yes (103)[a]	Yes (103)
Autopsy or death certificate only cases	Yes (34)	Yes (34)
Non–microscopically confirmed cases	Yes (83)	Yes (83)
Histologies for which AJCC 6th and 7th edition stage is not defined	Yes (425)	No
Code 988, blank for each SSF	No	Yes
Final sample size	11,176	11,601

Abbreviations: AJCC, American Joint Committee on Cancer; SEER, Surveillance, Epidemiology, and End Results; SSFs, site-specific factors.
[a] Numbers in parentheses show number of cases that were excluded.

International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3),[17] defines cancers of the corpus uteri by topography codes C54.0-54.3, 54.8, 54.9 and of uterus, NOS by ICD-O-3 topography code C55.9. The AJCC 7th edition classifies these cancers into 3 histological schema. Among diagnoses during 2010, corpus carcinoma (ICD-O-3 morphology codes 8000-8790, 8950, 8951, 8980-8981, 9700-9701) accounted for 11,821 cases (95.6%). An additional 478 cases (3.9%) were classified into the corpus sarcoma schema (ICD-O-3 morphology codes 8800-8932, 8934-8941, 8959-8974, 8982-9136, 9141-9582), and the remaining 60 cases (0.5%) belonged in the corpus adenosarcoma schema (ICD-O-3 morphology code 8933).

This report of AJCC 7th edition variables was restricted to malignant cancer cases belonging to the predominant schema, carcinomas of the corpus uteri. For the purpose of examining SSFs, 11,601 cases diagnosed in 2010 were included in the analytic cohort (Table 1) after 103 in situ cases were excluded because the updated FIGO staging system does not include this group, 113 cases were excluded because they were not microscopically confirmed, and 4 cases were excluded because they were diagnosed via autopsy or death certificate only.

The cohort for AJCC 6th and 7th edition staging comparisons was restricted to 11,176 cases after 425 additional cases with histologies not specified in the AJCC 6th

TABLE 2. SSFs for Corpus Uteri Cancer for AJCC 7th Edition Staging

SSF	Description	CS Version	Available for Analysis	Required by SEER
1	FIGO Stage	2	ydx 2010+	Yes
2	Peritoneal cytology	2	ydx 2010+	Yes[a]
3	Number of positive pelvic lymph nodes	2	ydx 2010+	Yes
4	Number of examined pelvic lymph nodes	2	ydx 2010+	Yes
5	Number of positive para-aortic nodes	2	ydx 2010+	Yes
6	Number of examined para-aortic nodes	2	ydx 2010+	Yes
7	Percentage of non–endometrioid cell type in mixed histology tumors	2	ydx 2010+	No
8	Omentectomy performed during first course of treatment	2	ydx 2010+	No

Abbreviations: AJCC, American Joint Committee on Cancer; CS, Collaborative Stage; FIGO, International Federation of Gynecology and Obstetrics; SEER, Surveillance, Epidemiology, and End Results; SSFs, site-specific factors; ydx, year of diagnosis.
[a] Required for compatibility with AJCC 6th edition staging.

edition were excluded (8980/3: carcinosarcoma, NOS, 411 cases; 8246/3: neuroendocrine carcinoma, 12 cases; and 8981/3: carcinosarcoma, embryonal type, 2 cases). Analyses of AJCC 6th edition staging trends included 60,204 cases with malignant corpus uteri and uterus, NOS cancer diagnosed during 2004-2010.

Key Changes Between the AJCC 6th and 7th Editions

The AJCC 7th edition includes in situ and preinvasive cases; however, the recent edition of the FIGO guidelines does not include in situ cases, and this report is restricted to malignant cancers only, which account for more than 99% of all reported cases. Research based on the AJCC 6th edition guidelines showed that stage IA (tumors confined to the endometrium) could not be distinguished reliably from stage IB (tumors that invade less than one-half of the myometrium), and in the 7th edition, they were combined as stage IA. Under the 7th edition, stage IB is reserved for tumors that invade one-half or more of the myometrium,[18] which were classified as stage IC under the 6th edition. Involvement in the endocervical glandular portion of the cervix was considered stage IIA under the AJCC 6th edition guidelines and is considered stage INOS, stage IA, or stage IB under the 7th edition. Involvement of the cervical stroma was classified as stage IIB in the AJCC 6th edition and remains stage II in the 7th edition.[19] The presence of cancer in ascites or peritoneal washings is downgraded from stage IIIA in the AJCC 6th edition to stages INOS, IA, IB, or II in the 7th edition because reports have shown that positive peritoneal cytology alone is not an independent prognostic factor if endometrial cancer is limited to the uterus.[20] In the AJCC 7th edition, cases with pelvic and para-aortic lymph node involvement were assigned to separate substages. Stage IIIC1 indicates positive pelvic nodes, and stage IIIC2 indicates positive para-aortic nodes with or without positive pelvic nodes, with the latter finding carrying a worse prognosis.[21,22] The emphasis on examination of lymph nodes is reflected in College of American Pathologists (CAP) guidelines.[23] Severity also varies by schema.[24] Studies have shown that malignant cytology is associated with a negative prognosis and a higher rate of recurrent disease.[25] The 7th edition no longer requires peritoneal cytology for staging but continues to recommend its collection as an SSF. This shift is likely to be related to an increasing body of evidence supporting positive peritoneal cytology as an adverse risk factor only if there is other evidence of extrauterine disease.[26]

Data regarding uterine sarcomas are not fully presented in this study. Sarcomas have a propensity for hematogenous spread and metastases. They were therefore placed in a separate schema from carcinomas in the AJCC 7th edition.[11,27] Carcinosarcoma (formerly known as malignant mixed Müllerian tumors) continue to be staged as carcinomas. Adenosarcoma of the uterus is a rare mixed neoplasm that includes both a benign epithelial component and a malignant stromal element. These tumors typically are polypoid masses that arise from the uterine fundus. Most adenosarcomas are diagnosed as stage I and generally carry a good prognosis.[24,28]

Summary of SSFs

Of 8 AJCC 7th edition SSFs introduced in 2010 for corpus uteri and corpus, NOS cancer (Table 2), 6 are required by the SEER Program for carcinoma, sarcoma, and adenosarcoma: FIGO stage (SSF1), peritoneal cytology results (SSF2), number of positive pelvic lymph nodes (SSF3), number of pelvic lymph nodes examined (SSF4), number of positive para-aortic lymph nodes (SSF5), and number of para-aortic lymph nodes examined (SSF6). Collection of SSF7 (percentage of non–endometrioid cell type in mixed histology tumors) and omentectomy (SSF8) were recommended by the AJCC but are not required by the SEER Program despite being included in the CAP cancer checklists.[23,24]

TABLE 3. Distribution of AJCC 6th and 7th Edition Staging System for Malignant Corpus Carcinoma, 2004-2010, SEER-18

Case Counts

Stage	2004	2005	2006	2007	2008	2009	6th 2010	APC	(95% CI)	7th 2010
Stage I										
INOS	456	477	503	519	527	577	557	3.7[b]	(2.4, 5.1)	631
IA[a]	1890	1929	1991	2023	2190	2382	2493	5.0[b]	(3.6, 6.5)	6027
IB[a]	2874	2958	2999	3250	3210	3326	3247	2.4[b]	(1.1, 3.7)	1482
IC	951	979	1033	1063	1127	1242	1369	6.2[b]	(4.6, 7.9	
Stage II										566
IINOS	131	115	99	91	119	115	164	3.7	(−5.2, 13.4)	
IIA	243	283	296	292	266	282	174	−2.9	(−10.8, 5.8)	
IIB	310	308	360	391	394	400	365	3.9	(0.0, 7.9)	
Stage III										
IIINOS	12	5	12	16	11	16	20	11.5	(−2.6, 27.7)	26
IIIA	389	421	432	484	510	623	594	8.3[b]	(5.5, 11.2)	312
IIIB	74	72	55	77	77	97	133	11.1[b]	(1.8, 21.3)	135
IIIC	544	584	665	672	701	768	797	6.4[b]	(4.9, 7.9)	
IIIC1										486
IIIC2										307
Stage IV										
IVNOS	8	4	8	12	10	5	2	−3.8	(−28.3, 28.9)	
IVA	69	63	73	66	63	67	77	1.2	(−2.5, 5.0)	79
IVB	579	559	562	603	641	616	669	2.8[b]	(1.0, 4.6)	669
Unknown	512	488	492	474	501	509	515	0.4	(−1.1, 1.9)	456
Total	9042	9245	9580	10,033	10,347	11,025	11,279	3.9[b]	(3.3, 4.5)	11,176

Percentage Distribution

Stage	2004	2005	2006	2007	2008	2009	6th 2010	7th 2010
Stage I								
INOS	5.0	5.2	5.3	5.2	5.1	5.2	5.0	5.7
IA[a]	20.9	20.9	20.8	20.2	21.2	21.6	22.3	53.9
IB[a]	31.8	32.0	31.3	32.4	31.0	30.2	29.1	13.3
IC	10.5	10.6	10.8	10.6	10.9	11.3	12.3	
Stage II								5.1
IINOS	1.5	1.2	1.0	0.9	1.2	1.0	1.5	
IIA	2.7	3.1	3.1	2.9	2.6	2.6	1.6	
IIB	3.4	3.3	3.8	3.9	3.8	3.6	3.3	
Stage III								
IIINOS	0.1	0.1	0.1	0.2	0.1	0.2	0.2	0.2
IIIA	4.3	4.6	4.5	4.8	4.9	5.7	5.3	2.8
IIIB	0.8	0.8	0.6	0.8	0.7	0.9	1.2	1.2
IIIC	6.0	6.3	6.9	6.7	6.8	7.0	7.1	
IIIC1								4.4
IIIC2								2.8
Stage IV								
IVNOS	0.1	0.0	0.1	0.1	0.1	0.1	0.0	
IVA	0.8	0.7	0.8	0.7	0.6	0.6	0.7	0.7
IVB	6.4	6.1	5.9	6.0	6.2	5.6	6.0	6.0
Unknown	5.7	5.3	5.1	4.7	4.8	4.6	4.6	4.1
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Abbreviations: AJCC, American Joint Committee on Cancer; APC, annual percent change; CI, confidence interval; NOS, not otherwise specified; SEER, Surveillance, Epidemiology, and End Results.

[a] Stages IA and IB were combined as stage IA in the AJCC 7th edition.

[b] $P < .05$.

Statistical Analysis

Database queries were performed with SEER*Stat v 8.0.2 (IMS, Calverton, MD). Annual percentage change in counts and 95% confidence intervals based on regression models were calculated using the SEER*Stat trend statistic option. Tables were populated using the FREQ procedure

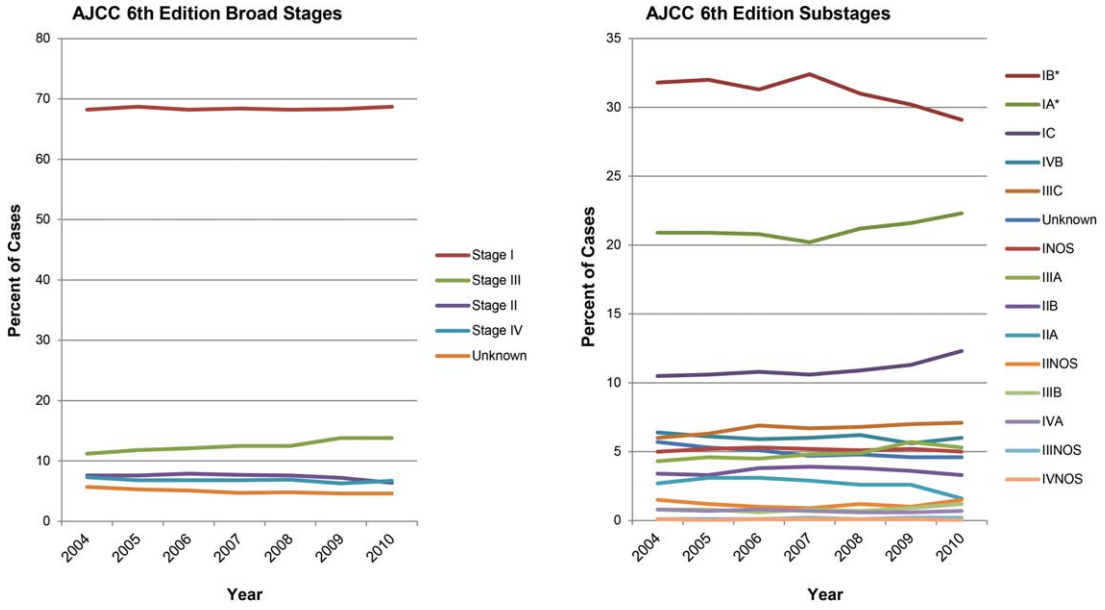

Figure 1. Trends in stage distributions for AJCC 6th edition staging system for malignant corpus carcinoma, 2004-2010, SEER-18. *Stages IA and IB were combined as stage IA in the AJCC 7th edition.

(SAS v 9.2, Cary, NC). Kappa statistics were calculated to assess agreement between AJCC 6th and 7th edition staging using the AGREE option of the FREQ procedure (SAS v 9.2, Cary, NC).

RESULTS

Cases

Trends in stage distributions for AJCC 6th edition corpus carcinoma, 2004-2010

Among microscopically confirmed malignant corpus carcinoma cases meeting AJCC 6th and AJCC 7th edition staging criteria, the number of cases diagnosed with malignant corpus carcinoma increased each year from 2004 through 2010 (APC, 3.7; 95% CI, 3.3-4.5; Table 3). Statistically significant increases in annual counts were also observed in the annual number of cases diagnosed at AJCC 6th edition stages INOS, IA, IB, IC, IIIA, IIIB, IIIC and IVB. Despite the increase in case counts, the annual percentage of stage I cases remained at about 68% each year, with shifts from substage IB to IA and IC (Fig. 1). The percentage of stage II cases dropped from 7.6% in 2004 to 6.4% in 2010, primarily because of a decrease in cases classified as stage IIA. The percentage of stage III cases increased from 11.2% in 2004 to 13.8% in 2010, with small increases in each substage. The percentage of cases staged as "unknown" decreased from 5.7% in 2004 to 4.6% in 2010.

Comparison of AJCC 6th and 7th edition stage distributions, corpus carcinoma, 2010

After exclusions, the AJCC stage comparison data set included 11,176 cases (Table 4). A total of 431 cases were moved from stages II and III according to AJCC 6th edition standards into stage I according to 7th edition criteria. In particular, endocervical glandular involvement was mapped to stage I in the 7th edition but not in the 6th (66.5% vs 63.0%), and fewer cases were classified as stages II or III in the 7th edition than in the 6th. Assessment of ascites and/or peritoneal washings also ceased to be used to define stage IIIA, resulting in fewer cases being classified as stage IIIA in the AJCC 7th edition compared with the 6th edition. Minimal changes occurred between the 6th and 7th editions for stage IV. Although staging agreement between the AJCC 6th and 7th editions is low (44%) overall, this primarily reflects the structural changes within stages I, II, and III.

SSFs

After exclusions, the SSF data set included 11,601 cases of carcinomas of the corpus uteri diagnosed in 2010 according to AJCC 7th edition criteria (Table 5). The majority of these cases (68.3%) were diagnosed with endometrioid adenocarcinoma (ICD-O-3 morphology code 8380), with 46 other reported histologies (data not shown).

Table 5 lists not applicable and applicable codes for analysis of the 6 SSFs. Applicable codes are further

TABLE 4. Distribution of AJCC 6th by 7th Edition Staging System for Malignant Corpus Carcinoma, 2010, SEER-18

Case Counts

Stage AJCC 6	AJCC 7											
	INOS	IA	IB	II	IIINOS	IIIA	IIIB	IIIC1	IIIC2	IVA	IVB	Unknown
INOS	557											
IA[a]		2493										
IB[a]		3247										
IC			1369									
IINOS				164								
IIA	55	80	39									
IIB				365								
IIINOS					17	2						1
IIIA	16	177	64	35		302						
IIIB							133					
IIIC								483	304			10
IVNOS										2		
IVA										77		
IVB											669	
Unknown	3	30	10	2	9	8	2	3	3			445
Total	631	6027	1482	566	26	312	135	486	307	79	669	456

Percentage Distribution

Stage AJCC 6	AJCC 7											
	INOS	IA	IB	II	IIINOS	IIIA	IIIB	IIIC1	IIIC2	IVA	IVB	Unknown
INOS	88.3											
IA[a]		41.4										
IB[a]		53.9										
IC			92.4									
IINOS				29.0								
IIA	8.7	1.3	2.6									
IIB				64.5								
IIINOS					65.4	0.6						0.2
IIIA	2.5	2.9	4.3	6.2		96.8						
IIIB							98.5					
IIIC								99.4	99.0			2.2
IVNOS										2.5		
IVA										97.5		
IVB											100.0	
Unknown	0.5	0.5	0.7	0.4	34.6	2.6	1.5	0.6	1.0			97.6
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Abbreviations: AJCC, American Joint Committee on Cancer; NOS, not otherwise specified; SEER, Surveillance, Epidemiology, and End Results.
[a] Stages IA and IB were combined as stage IA in the AJCC 7th edition.

stratified into known and unknown values. All cases are "applicable" for FIGO Stage and Peritoneal Cytology because data would be expected on each case. However, the percentage of "not applicable" ranges from 37.3% to 64.1% for variables related to pelvic and para-aortic lymph node involvement because lymph nodes are most likely to be examined when biopsy or surgery is performed. Cases coded as "not applicable" were excluded from "known" versus "unknown" analyses for the SSFs.

SSF1: FIGO stage, corpus carcinoma

According to the Collaborative Stage (CS) Data Collection System coding instructions, FIGO stage is recorded as it was documented by the clinician or pathologist in the medical record. If it is not mentioned, an unknown value (999) is assigned. Of the eligible corpus carcinoma cases diagnosed in 2010, FIGO stage was known for 69.2% and unknown for 30.8% of cases, with the majority of known cases in stage I subgroups or stage II (Table 6). FIGO stage also can be

TABLE 5. Known and Unknown Values for Malignant Corpus Carcinoma SSFs, SEER, 2010 Cases

	Not Applicable			Among Applicable						
				Known			Unknown			
SSF	Codes	n	%	Codes	n	%	Codes	n	%	Total n
1. FIGO Stage	888, 988	0	0.0	100-420	8025	69.2	987, 999	3576	30.8	11,601
2. Peritoneal cytology[a]	888, 988	0	0.0	000,010	7115	61.5	020, 997, 998, 999	4486	38.7	11,601
3. Number of positive pelvic nodes	098, 888, 988	4323	37.3	000-097	6966	95.7	999	312	4.3	7278
4. Number of examined pelvic nodes	000, 888, 988	4571	39.4	001-090	6372	90.6	095-098,999	658	9.4	7030
5. Number of positive para-aortic nodes	098, 988	6965	60.0	000-097	4268	92.1	999	368	7.9	4636
6. Number of examined para-aortic nodes	000, 988	7434	64.1	001-090	3354	80.5	095-098,999	813	19.5	4167

Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; SEER, Surveillance, Epidemiology, and End Results; SSFs, site-specific factors.
[a] Required for staging.

TABLE 6. Distribution of SSF1: FIGO Stage for Malignant Corpus Carcinoma 2010, SEER

FIGO Stage	CS Code	Cases, n	Frequency (%)
Total		11,601	100
I (NOS)	100	1658	14.3
1A	110	2897	25.0
1B	120	992	8.6
II	200	1046	9.0
III (NOS)	300	296	2.6
IIIA	310	299	2.6
IIIB	320	120	1.0
IIIC (NOS)	330	89	0.8
IIIC1	331	190	1.6
IIIC2	332	134	1.2
IV (NOS)	400	54	0.5
IVA	410	52	0.5
IV	420	198	1.7
Unknown	987, 999	3576	30.8

Abbreviations: CS, Collaborative Stage; FIGO, International Federation of Gynecology and Obstetrics; NOS, not otherwise specified; SEER, Surveillance, Epidemiology, and End Results; SSF, site-specific factor.

TABLE 7. Distribution of SSF2: Peritoneal Cytology for Malignant Corpus Carcinoma, 2010, SEER

Result of Peritoneal Cytology	CS Code	Case Count	Frequency (%)
Total		11,601	100.0
Negative	0	6284	54.2
Positive, malignant cells positive	10	831	7.2
Tested but undetermined, unknown	20, 997-999	4486	38.7

Abbreviations: CS, Collaborative Stage; SEER, Surveillance, Epidemiology, and End Results; SSF, site-specific factor.

derived from other stage data that are collected by the SEER Program. A comparison of SSF1, the collected FIGO stage, with AJCC 7th edition group stage found moderate agreement between the two variables (kappa, 0.55).

TABLE 8. Distribution of SSF3: Number of Positive Pelvic Lymph Nodes for Malignant Corpus Carcinoma, 2010, SEER

Assessment of Pelvic Lymph Nodes	Case Count	Frequency (%)
Total	7278	100.0
Nodes negative	6070	83.4
1 Positive node	348	4.8
2 Positive nodes	204	2.8
3 Positive nodes	106	1.5
4 Positive nodes	62	0.9
5 Positive nodes	30	0.4
6 or More positive nodes	112	1.5
Positive aspiration/core biopsy	7	0.1
Positive number unknown	27	0.4
Unknown	312	4.3
(Not Applicable)	(4323)	

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; SSF, site-specific factor.

SSF2: Peritoneal cytology, corpus carcinoma

The presence of cancer cells in ascites or peritoneal washings was a criterion for stage IIIA classification in the AJCC 6th edition. Studies had shown that malignant cytology was associated with a negative prognosis and a higher rate of recurrent disease.[25,26] Despite not being part of the 2008 FIGO staging system, data were known for 61.5% of corpus carcinoma cases. Table 7 indicates that 54.2% of the 2010 cases had negative peritoneal cytology, 7.2% had positive peritoneal cytology, and data were unavailable for almost 38.7% of cases.

SSF3: Pelvic nodes positive

There were 4323 cases (37.3%) for whom SSF3 was not applicable (Table 5). Of the 7278 cases with pelvic lymph nodes assessed, 6966 (95.7%) had known values. Of these 7278 cases with pelvic lymph nodes assessed, 83.4% were

TABLE 9. Distribution of SSF4: Number of Pelvic Lymph Nodes Examined for Malignant Corpus Carcinoma, 2010, SEER

Number of Pelvic Lymph Nodes Examined	Case Count	Frequency (%)
Total	7030	100.0
1-10	2830	40.3
11-20	2382	33.9
21-30	810	11.5
31-89	350	5.0
90+	0	0.0
No pelvic lymph node removed, but aspiration of pelvic nodes performed (95)	23	0.3
Pelvic lymph node removal, but number of nodes unknown (96, 97, 98)	324	4.6
Unknown (999)	311	4.4
(Not applicable)	(4571)	

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; SSF, site-specific factor.

TABLE 10. Distribution of SSF5, Number of Positive Para-Aortic Lymph Nodes, Malignant Corpus Carcinoma, 2010, SEER

Assessment of Para-Aortic Lymph Nodes	Case Count	Frequency (%)
Total	4636	100.0
Nodes negative	3836	82.7
1-10 Nodes positive	373	8.1
11-20 Nodes positive	30	0.7
21-30 Nodes positive	2	0.0
31-89 Nodes positive	3	0.1
90+ Nodes positive	0	0.0
Positive aspiration or core biopsy of para-aortic lymph node(s)	6	0.1
Positive para-aortic lymph nodes, number not specified	18	0.4
Unknown	368	7.9
(Not applicable)	(6965)	

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; SSF, site-specific factor.

classified as negative, 12.4% were classified as positive, and the result of the assessment was classified as unknown for 4.3% of the cases (Table 8).

SSF4: Pelvic nodes examined

SSF4 was not applicable for 4571 cases (39.4%); see Table 5. This variable was applicable to 7030 cases, and 6372 (90.6%) of them had known values. Among cases for which pelvic nodes were examined, 40.3% were classified as having between 1 and 10 nodes examined, and 33.9% were classified as having had between 11 and 20 nodes examined (Table 9). Analysis of the number of nodes examined by grade showed that cases with poorly or undifferentiated cancer were more likely to have dissected pelvic nodes examined than those with moderately or well-differentiated tumors ($P < .001$, data not shown).

TABLE 11. Distribution of SSF6, Number of Para-Aortic Lymph Nodes Examined, Malignant Corpus Carcinoma, 2010, SEER

Number of Para-Aortic Lymph Nodes Examined	Case Count	Frequency (%)
Total	4167	100.0
1-10	2861	68.7
11-20	410	9.8
21-30	60	1.4
31-89	21	0.5
90+	2	0.1
No para-aortic nodes removed, but aspiration of para-aortic nodes performed (95)	53	1.3
Para-aortic lymph node removal with unknown number of nodes (96-98)	390	9.4
Unknown	370	8.9
(Not applicable)	(7434)	

Abbreviations: SEER, Surveillance, Epidemiology, and End Results; SSF, site-specific factor.

SSF5: Para-aortic nodes positive

SSF was not applicable to 6965 cases (60%). The variable was applicable to 4636 cases, and 4268 (92.1%) had known values. Of the 4636 cases with para-aortic nodes assessed (SSF 5), 82.7% were classified as having cancer-negative nodes, 9.4% were classified as having positive nodes, and the information was unknown for 7.9% of the cases (Table 10).

SSF6: Para-aortic nodes examined

Regarding SSF6, para-aortic nodes were not examined in 64.1% of cases (Table 5). Among cases for which para-aortic nodes were examined, 68.7% were found to have had between 1 and 10 nodes examined, and 9.8% had between 11 and 20 nodes examined (Table 11). Analysis of the number of nodes examined by grade showed that cases with poorly or undifferentiated cancer were more likely to have had dissected para-aortic nodes examined than those with moderately or well-differentiated tumors ($P < .001$, data not shown).

DISCUSSION

In the 7th edition of the AJCC, SSFs were incorporated for the first time, and extent of disease was expanded beyond anatomic extent alone. This reflects new insights regarding predictive and prognostically significant information. Of the 6 SSFs that currently are collected by the

SEER Program for corpus carcinoma, 5 appear to be suitable for analytic purposes, and we recommend that FIGO staging be derived and no longer collected from the medical record. Staging differences between the AJCC 6th and 7th editions resulted in some downstaging of corpus carcinoma. The quality of the lymph node data may reflect a divergence between clinical practice and American Congress of Obstetricians and Gynecologists (ACOG) and FIGO guidelines. Specifically, despite the recommendations that all patients have lymph node dissections, SEER data indicate that lymph nodes were more likely to be biopsied when patients had poorly differentiated cancers. Additional prognostic factors that could be considered as SSFs for corpus uteri and corpus, NOS include lymph vascular invasion.[29]

The ACOG guidelines state that retroperitoneal lymph node assessment is a critical component of surgical staging.[9] Patients without lymph node involvement may avoid adjuvant therapy and radiation. Both para-aortic and pelvic lymph node beds should be evaluated because retroperitoneal palpation is inaccurate and sentinel lymph node biopsy or pelvic lymph node sampling alone is unacceptable. Isolated para-aortic metastases are reported in up to 17% of patients. Lymph nodes may not be sampled when women with complex hyperplasia are diagnosed with uterine corpus cancer without surgical staging. Obesity also can impede access to the retroperitoneal space, and prolonged surgery may not be indicated for patients with severe comorbidities. Lymphedema, a chronic condition affecting a small percentage of women, also can influence decisions to perform a thorough lymph node dissection during uterine cancer surgery.

Analysis of the number of nodes examined by grade showed that cases with poorly or undifferentiated cancers were more likely to undergo pelvic and para-aortic node dissections than those with moderately or well-differentiated cancers. This finding suggests that clinicians are particularly likely to obtain this information when patients have high-grade tumors.

Of the 3 uterine corpus cancer schemas, carcinomas account for more than 95% of cases, with an annual incidence rate approaching 25 per 100,000 women in 2010.[2] Trends for all uterine corpus and corpus, NOS cancers therefore mirror those for corpus carcinomas. Annual incidence rates of sarcoma and adenosarcoma were lower, in the range of 1 case per 100,000 women and 1 case per million women, respectively. In all 3 schemas, a handful of histologies account for a large proportion of cases. For carcinoma, the predominant histology was endometrioid carcinoma, followed by adenocarcinoma, NOS. For sarcoma, leiomyosarcoma, NOS was the main histology. Adenosarcoma was the sole histology in the third schema. We are unaware of major changes in ICD-O-3 codes for uterine corpus; however, subtle shifts in histologies are possible, and caution is warranted when assessing temporal trends by schema. Limitations include the collection of data in SEER registries only. These registries cover only 28% of the United States, and tend to have a higher proportion of foreign-born persons than the general US population.

In summary, some downstaging occurred in conversion from the AJCC 6th to the 7th edition. Most SSFs collected by SEER are suitable for analysis. The paucity of data on lymph nodes, with more responses among cases with high-grade cancer, may reflect when lymph node dissections are performed. Follow-up for survival can be used to assess SSF predictive value.

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CONFLICT OF INTEREST DISCLOSURES

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